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## THE EXTRA PHARMACOPŒIA



# THE EXTRA PHARMACOPŒIA

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MARTINDALE

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*Twenty-first Edition*  
IN TWO VOLUMES



## VOLUME I

Published by direction of  
the Council of the  
Pharmaceutical Society of Great Britain

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## PREFACE

The publication of Volume I of the Twenty-First Edition of the *Extra Pharmacopœia* will remind "Martindale" readers that the First Edition of this survey of substances used for the treatment of human ailments and diseases was written in 1883 by William Martindale and W. Wynn Westcott and that, following the death in 1933 of William Harrison Martindale, the responsibility for its continued production was taken over by the Council of the Pharmaceutical Society of Great Britain.

At this important and outstanding period of the history of the book, it is of interest to mention and record that the first ten volumes were produced under the joint Editorship of William Martindale and W. Wynn Westcott. The former died in 1902 and his son, William Harrison Martindale, carried on the work through eight more editions with Dr Westcott, until the death of the latter in 1925. The nineteenth and twentieth editions, published in 1928 and 1932 respectively, were issued by the late William Harrison Martindale with the aid of occasional assistance from medical friends on points of difficulty, and the intense personal attention devoted by him to the yearly increasing task of revision undoubtedly contributed to his death. Reference must be made also to the change of publishers, which has terminated a long association between former publishers and the *Extra Pharmacopœia*; previous editions have been published by Messrs. H. K. Lewis & Co Ltd, whereas this edition is published by the Pharmaceutical Press.

The responsibility for further revision was delegated by the Council to the British Pharmaceutical Codex Revision Committee and the Editor of the *Codex*, Mr. C. E. Corfield, was appointed Editor of "Martindale." Under this new arrangement, Volume II of the Twentieth Edition, which is concerned mainly with matters of diagnosis, with the analysis and assay of medical products, and with numerous other subjects associated with medicine, chemistry and pharmacy not included in the first volume, was produced in 1935. In the preface to this volume readers were reminded that Martindale's *Extra Pharmacopœia* had owed much to the self-sacrificing personal labours of William Martindale and of W. H. Martindale in producing a working summary of the literature on original work and notable advances throughout the whole field of therapeutics. It was recognised that these authors had "animated the whole work with an undefinable personality which expressed itself at times in *ex cathedra* judgments of a refreshing directness, and at others in the warnings of an experienced and well-informed mind against the stampede of novelty."

To-day it is necessary to record an increasingly wide field of therapeutic agents and to review an ever-increasing bulk of scientific literature. This has made the continuance of revision

by an individual an impossibility and has necessitated a revision of the work by an organisation having medical, pharmaceutical and chemical experts, and having no direct commercial interests. Thus, the *Extra Pharmacopœia* will continue to meet that need in medicine and in pharmacy of a comprehensive summary of the composition and applications of the multitude of old and new, official and proprietary substances about which the doctor or the pharmacist may require information.

In this new Edition a large proportion of the matter has been rearranged and rewritten, and the whole of the material has been examined exhaustively with the object of removing matter of little or no value and replacing it by useful accounts of the many new substances or modern applications which have been introduced during the last four years. Every effort has been made to give information on all the compounds and preparations which the doctor uses or is recommended to use for the treatment of his patient, including notes on their composition and practical observations on the results of their application, and to provide the dispenser with that general and practical knowledge of the constitution and properties of the chemical, animal and vegetable drugs, which is necessary for him to prepare and dispense successfully the prescriptions of the medical practitioner in both hospital and private practice.

### **Classification**

The increase in the number of medicinal substances resulting from the researches of the chemist, the pharmacist, the pharmacologist and other investigators in the laboratories of the manufacturers, the hospitals or other institutions, has necessitated a change in the classification and arrangement of the book, so as to bring together substances which are either somewhat similar or clearly related in constitution, and to group, as far as possible, those substances which have similar therapeutic or pharmacological action and are used for similar purposes.

The classification, as in previous editions, is based upon the selection of parent substances in common use which serve to form sections of the book, and thus enable readers to review a group of medicinal agents of related composition or medicinal action with the minimum amount of inconvenience. These principal or parent substances are arranged alphabetically, and in each section are included those compounds which are chemically related and those substances which, although not having a close connection by constitution or origin, bear a somewhat similar pharmacological action or are frequently used for the treatment of the same ailment or disease. For example, the several official barbiturates are grouped under the heading "*Barbitonum*," and in this section will be found all the information concerning the many well-known proprietary and non-proprietary barbiturates, together with closely related substances, their more complex derivatives and the compounded preparations which depend for their action wholly or

partly upon the presence of one of these powerful hypnotics. Similarly, under the heading "*Arsenum*" is a section arranged to provide the reader with a systematic account of the information which is necessary to understand the composition, properties and application of the simple inorganic arsenic compounds and the complex organic arsenicals such as Tryparsamide and Neoarsphenamine.

The extension of this system has resulted in modifications in several of the headings familiar to readers of earlier editions. The section on "*Coal Tar Derivatives*," which previously contained the descriptions of the flavine antiseptics and a small but miscellaneous collection of dyes and synthetic chemicals, has been discontinued, and the necessary information included under more appropriate headings. The section on "*Nutrimenta*," which contained brief accounts of various milk and other food products, and of the vitamins and commercial vitamin preparations, has been replaced by more complete and systematic notes in more convenient sections. Similarly, it has been deemed undesirable to continue the inclusion of the several important hormones and glandular products of animal origin in one section under "*Animal Organotherapy*." The rapidly increasing importance in therapeutics of posterior and anterior pituitary, thyroid and parathyroid, the male and female hormones, liver and stomach extracts, make it necessary to increase considerably the information given on these substances, and in this edition Adrenaline, Liver Extracts, Insulin, Estrin, Pituitary, and Thyroid are placed in separate sections in a manner similar to the inclusion of Insulin in previous editions. The introduction of new therapeutic agents and the discovery of new applications for some of the older products have resulted in a drastic alteration in the manner of presenting the information which in previous editions was included in a section under the heading "*Supplementary List of Drugs*." In order to avoid increasing unduly the size of the volume, notes which may not have been of much value to readers have been deleted, in some cases the inclusion of extended notes on an older drug would have made a supplementary list inconvenient and often ambiguous. The new classification has made it possible to decrease the notes on some products previously dealt with in other sections without transferring them to a supplementary list, as well as to emphasise the value of certain products mentioned in the old list. The substances mainly concerned in this respect are vegetable drugs which are still given a place in National Pharmacopœias, and have accepted therapeutic properties, and in which the absence of a separated chemical constituent does not appear to justify their entire deletion or even their relegation to a position of almost complete obscurity. The section dealing with "*Vaccines and Sera*" remains as a separate chapter, because in this form the information appears to be of greater value to the doctor who is concerned with the treatment of a particular disease, and for this reason the notes are arranged mainly under the sub-headings of diseases in



preference to dealing separately with individual Antitoxins, Sera, Toxins and Vaccines.

### ***New Pharmacopœias and Formularies***

Since the publication of the Twentieth Edition several new Pharmacopœias have been produced, including the *United States Pharmacopœia XI*, the *Swiss Pharmacopœia V*, and the *Danish Pharmacopœia*, 1933. An *Addendum*, 1936, to the *British Pharmacopœia*, 1932, has been published recently. In addition, new editions of some established Formularies have appeared, including the *National Formulary of Unofficial Preparations* issued by the American Pharmaceutical Association, *N.F. VI*, 1936, and the *British Pharmaceutical Codex*, 1934, as well as new editions of several hospital pharmacopœias. All these publications have been examined, and the *Extra Pharmacopœia* has been revised so as to bring it into line with the new volumes. The articles and preparations of the *B.P.* 1932 now replace those of the *B.P.* 1914, instead of being included in a synopsis, and many of the isolated combinations of previous editions have been replaced by the recognised formulæ of the *British Pharmaceutical Codex* or by accepted formulæ from the pharmacopœias of the principal London and provincial hospitals.

### ***Abbreviations and Nomenclature***

In earlier editions, the cubic centimetre has been used as the unit of volume in the metric system for expressing the doses of liquids and volumes of liquids in various formulæ; the abbreviation used was *Cc.* In this edition the cubic centimetre has been replaced by the millilitre, which is the recognised international unit adopted in both the *British Pharmacopœia* and the *British Pharmaceutical Codex*, and which is common to all scientific literature in Great Britain; the abbreviation used is *ml*. Likewise the abbreviation *Gm.* for gramme has been replaced by *g.*, which is the abbreviation recommended and used by the editors of the principal scientific publications. Doses are given in both metric and Imperial systems, as in previous editions, but the abbreviations *gr* for grain and *m* for minim are used only in formulæ or when doses occur in a descriptive paragraph, or in abstracts from the literature.

The nomenclature adopted throughout the book is based upon that of the *B.P.* and the *B.P.C.*, and thus the book contributes towards the general adoption of a uniform system, which is always helpful to both the prescriber and the dispenser. Nevertheless, it will probably be a long time hence before an international nomenclature is accepted, and the dispensing of foreign prescriptions thereby simplified, and one does not foresee in the near future the adoption of any uniform system by proprietary medicine manufacturers by which the doctor or the public may more easily understand the constituents named in their disclosed formulæ.

### ***Synonyms and Proprietary Names***

In addition to the official or general name of the substance, commonly used synonyms are given, as well as the trade names

which indicate the products of particular manufacturers. The doctor will thus be able to see immediately whether he is prescribing a well-known drug under an official name or under a proprietary name, and the pharmacist is provided with the knowledge which enables him to understand when a non-proprietary product may be dispensed and when it is not permissible to dispense a non-proprietary equivalent on a prescription for the product of a particular factory. Coupled with these proprietary names is an indication of the source of the article, whether of British or foreign manufacture perhaps, and the name of the firm or firms from which supplies or further information can be obtained. The inclusion of the names of these proprietary forms of a drug is an important feature of the *Extra Pharmacopœia*, and provides practically the only concise information available to the doctor by which he can discover whether many of the so-called ethical proprietaries are new products of the research laboratory, or simply older chemicals or preparations making a new appearance in a modified form. In this edition the asterisk and registration numbers have been replaced by the name of the manufacturer and/or agent, and the town, a system which has been tried out in an appendix to the *BPC* 1934, and since proved by usage to be of the utmost value to both doctor and pharmacist.

A similar system is adopted for chemical compounds and preparations of chemical or animal substances which have no common equivalent, and which are available to the prescriber and the dispenser only under the registered name of the maker. Thus, the user is provided with information on nearly every branded product which is available to medicine and pharmacy. In the majority of cases the notes included have been taken from literature issued by the respective makers or agents; they include, in general, an indication of the composition, the therapeutic use and the usual dose, with any abstracts from the literature having important bearing on its use for the treatment of the disease for which it has been recommended. In presenting this information to the doctor, it is necessary to remind him that a very large number of important contributions to the physician's resources come from the laboratories of manufacturing chemists who very naturally protect their interests by patents and trade-marks. At the same time the dispenser must be reminded that when a substance is ordered under its trade-mark description it is an actionable infringement to supply a product of another maker. A reference to the pages dealing with the barbitone group of hypnotics, the organic arsenicals, or the pituitary products will suffice to show that the new volume is an invaluable guide to both doctors and pharmacists in connection with all drugs of a proprietary character.

### ***Poisons and Dangerous Drugs***

In previous editions, the *Extra Pharmacopœia* has provided the doctor and the pharmacist with a complete guide to the application of the existing law to the sale and supply of "poisons"

and "dangerous drugs" Every substance or preparation was marked so as to indicate clearly whether it was a Schedule I or a Schedule II poison. In this edition, following the coming into force of the Poisons Rules, 1935, governing the distribution of substances contained in the Poisons List prepared for the purpose of administering the Pharmacy and Poisons Act, 1933, this service is continued, and every effort has been made to apply this much more complicated system of control to the individual preparations and substances described in the book To-day poisons are in one of two parts of the List, and the Rules contain a number of schedules which determine the special restrictions, exemptions, or other conditions which apply to the various groups

At the beginning of each section containing a group of poisons, the corresponding item in the Poisons List is quoted and its position marked by [P1] for part I or [P2] for part 2 Similarly, items from the schedules appended to the Poisons Rules are given to indicate whether the sale or supply of substances in the group are subject to any special restrictions or exemptions The least complicated system possible has been devised for this purpose, and readers should note that the symbols [S1] and [S4], for example, refer respectively to Schedules I and IV of the Rules Dangerous drugs are indicated by the symbol [D] Preceding the names of substances which are poisons, readers will observe symbols or groups of symbols, from which they obtain without effort a concise summary to the conditions which apply Thus, [P1 S1] tells him that he is concerned with a Part I poison, subject to the special restrictions governing the poisons in Schedule I Likewise, [P1 S1 S4] indicates that the substance is in Part I of the Poisons List, that it is included in Schedules I and IV and, consequently, supplied to the public only by authorised sellers on the prescription of a doctor, dentist or veterinary surgeon

### ***Some Important Therapeutic Agents Described***

The following notes give a brief indication of some of the many important substances dealt with and draw attention to a few of the new therapeutic agents described

**ACIDUM ACETYSALICYLICUM** The composition, with proprietary names, of official substances, so-called ethical proprietaries, and advertised remedies, *p.* 14

**ACIDUM MANDELICUM** The treatment of urinary infections with preparations of the acid and its salts, *p.* 24

**SODII THIOSULPHAS.** The prevention and treatment of stomatitis due to injections of mercury, bismuth, or arsenic, *p.* 103

**ACIDUM TANNICUM** Its application and value for the treatment of burns, *p.* 104

**ACRIFLAVINA.** The prevention of sepsis in wounds with acriflavine, euflavine and proflavine preparations, *p.* 115

**ADRENALINA.** A full account of its uses, with summaries of the composition of the various combinations recommended, *p.* 125.

**KAOLINUM** The various brands of colloidal kaolin for gastric and intestinal affections, including references to magnesium trisilicate, *p* 165

**ANTIMONII ET SODII TARTRAS** The use of organic antimony compounds in leishmaniasis, kala-azar, bilharziasis, etc., *p* 182

**ARGENTOPROTEINUM** The composition of the various types of colloidal silver and their use as non-irritant antiseptics, *p* 191

**ARSENUM** An exhaustive account of inorganic and organic arsenicals, including acetarsol, tryparsamide and the arsphenamines, *p* 195

**AURI ET SODII THIOSULPHAS** The gold compounds introduced for the treatment of tuberculosis and rheumatoid arthritis, *p* 240

**BARBITONUM** The composition and characters of all the important members of the wide field of barbiturates, *p* 253

**CALCII GLUCONAS** The calcium compound preferred for painless intramuscular injection, *p* 309

**CASEINUM** A useful summary of the composition of many proprietary infants' and invalids' foods, *p* 344

**PULVIS VITAMIN B<sub>1</sub>** Opinions and claims regarding the therapeutic value of this antineuritic vitamin, *p* 351

**CHLOROFORMUM** The anæsthetic uses and preparations of chloroform, with notes on the anæsthetic hydrocarbons, *p* 365

**CINCHOPHENUM** The composition and toxic effects of these widely used and dangerous drugs, *p* 378

**COCAINA** A summary and analysis of the enormous group of official and proprietary local anæsthetics, *p* 384

**DIGITALIS** The glycosides and standardised preparations available for the treatment of heart diseases, *p* 440

**EPHEDRINA** The action of the ephedrine alkaloids and the composition of commercial substances containing them, *p* 452

**ERGOIA** Ergometrine and the other new alkaloids of ergot—their composition, pharmacology, and clinical uses, *p* 458

**HISTAMINÆ PHOSPHAS ACIDUS** The new official salt used in the treatment of rheumatism, *p* 465

**HISTIDINE HYDROCHLORIDE** Opinions and experiences concerning its action in the treatment of peptic ulcers, *p* 467

**HEPAS** A concise description of liver extracts and stomach products for pernicious anæmia, including the various proprietary preparations available, *p* 517.

**HYDRARGYRUM** The mercury preparations and compounds used for syphilis, and the new Mersalyl for cardiac œdema, *p* 534.

**INSULIN** Up-to-date information on the administration of this hormone essential to the life of diabetic sufferers, *p* 571

**IODUM** The composition of the iodine preparations and compounds for X-ray diagnosis and for internal use by mouth and by injection, *p* 586

**EMETINA** The treatment of amœbic dysentery by the administration of emetine salts with bismuth, arsenic, etc., *p* 600

**LIGATURES** A brief account of surgical ligatures and sutures, with notes on their sterilisation, *p* 613.

**MORPHINA.** A summary of the principal factors related to the treatment of morphine addicts. "D.D A" and "[P1 81]" poisons are clearly indicated, p. 637.

**ŒSTRINUM.** Under this heading the male and female hormones are described, and the numerous proprietary products which depend for their action upon these bodies are summarised, p. 658.

**OLEUM HYDROCARI.** The varieties and derivatives used in the treatment of leprosy are described, p. 680

**OLEUM MORRHUÆ.** Calciferol, halibut-liver oil, and vitamin A and D preparations generally are summarised in this section, p. 685.

**PEPTONUM.** The subject of non-specific protein therapy and the numerous substances used for producing protein shock, p. 725

**PHENOL.** The composition of all its preparations and their classification as poisons; the complications of the Poisons List and the restrictions and exemptions of the schedules to the Poisons Rules have been minutely applied, p. 744

**DINITROPHENOLS** The nitro-compounds which have been used for the reduction of obesity, with results arising therefrom, p. 753.

**IODOPHTHALEINUM.** Its intravenous and oral administration for producing opacity of the gall-bladder to X-rays, p. 756

**PHYSOSTIGMINA.** The synthetic peristaltic stimulant, Prostigmin, related to physostigmine, is described, p. 760.

**PITUITARIUM** The active principles of the anterior and posterior pituitary lobes are explained, and the many proprietary products are described or compared, p. 784

**CHINIOFONUM.** The official substance, better known as Yatren, for acute and chronic amœbic dysentery, p. 797

**QUININA** Descriptions of all the quinine compounds; their use in malaria and, with urethane, for varicose veins; descriptions and references relating to synthetic anti-malarials such as Quino-Plasmoquine, Atebrin and Atebrin-Musonate, p. 809.

**STRAMONIUM.** The preparations of stramonium used in the treatment of parkinsonism, p. 861

**THYROIDEUM** The actions of the thyroid constituents are explained and the proprietary substances containing thyroid and related substances are summarised, p. 889

**UREA.** The symmetrical ureas and related compounds administered for trypanosomiasis, gonococcal, streptococcal and other infections; results with Prontosil and Prontosil S are included, p. 906.

### ***Vaccines, Toxins and Antitoxins***

It has been deemed desirable to retain the arrangement of former editions in which preparations derived from bacteria or from the products of bacterial growth are dealt with collectively in one section of the book. This section is introduced by a general account of the principles underlying the use of bacterial antigens and a description of the nature and preparation of vaccines, anti-

viruses, bacteriophages, toxins, antitoxins, etc. As far as possible, individual substances belonging to these groups are dealt with under the diseases for which they are used. The administration of vaccines by mouth must still be regarded as in the experimental stage; references to some clinical trials are given under Oral Cold Vaccine, Dysentery Vaccine, Typhoid Vaccine and B.C.G. Vaccine. The subject matter relating to the Schick Test and active immunisation against diphtheria, and that relating to the Dick Test and active immunisation against scarlet fever, included in Volume II of the Twentieth Edition, has been transferred, with additions, to the present volume. The literature relating to Meningococcus Antitoxin, the serum treatment of pneumonia, the use of Snake Venom in hæmophilia, Cobra Venom as an analgesic in cancer and in the treatment of epilepsy, and reports on the vaccine prophylaxis and treatment of whooping cough, have been abstracted. The use of Staphylococcus Antitoxin, Staphylococcus Toxoid and Tetanus Toxoid are amongst other additions to this section, the whole of which has been revised in the light of recent reports.

### ***Summaries of Legal Requirements***

The pages at the end of the volume contain a practical summary of the Poisons Rules, 1935, in which the reader is provided with a concise account of the conditions governing the sale or supply of poisons by the doctor, dentist or veterinary surgeon, the pharmacist, the wholesaler and the hospital. This section also contains for purposes of reference the various schedules appended to the Rules, the schedules of poisons applicable to Northern Ireland and the Irish Free State, a summary of Dangerous Drug legislation which outlines the principal points to be remembered by the prescriber and dispenser, and a summary of the regulations made under the Therapeutic Substances Act, 1925, which provides for the regulation of the manufacture, sale, and importation of vaccines, sera and other therapeutic substances, such as the organic arsenicals of the arsphenamine group, insulin and pituitary (posterior lobe) extract.

### ***Therapeutic Index***

The Therapeutic Index has been subjected to exhaustive examination, and is reproduced in a modified and much improved form. A large proportion of the references to treatment have been transferred to their rightful places in the main part of the book, many additions have been made so as to bring the index into line with modern treatment of disease with newer drugs, and greater emphasis in the list has been given to the grouping of drugs in accordance with their pharmacological action. The doctor requires an index of this character as a general guide to the different drugs which at various times have been used in connection with a particular ailment or disease, or to groups of drugs which have a somewhat similar pharmacological action. He is recommended to

use the index only as a guide to treatment by drugs, and to refer to the summary of their uses and the different forms of administration in the body of the book

### ***Antidotes to Poisons***

Other sections of the work in which changes of interest have been made include the revised brief accounts of the important subjects of Blood Transfusion and Antidotes to Poisons. Much useful information has been added to the notes on antidotes under the substances which behave as powerful poisons, and the paragraphs will be of increased value to medical men who are called upon to treat cases of poisoning

### ***Acknowledgments***

Throughout the revision the fullest use has been made of medical and pharmaceutical literature, and as far as possible care has been taken to select matter which is likely to be of most value to the doctor and the pharmacist. In reviewing such a wide range of pharmacopœias, formularies, and literature, it is probable that some point of importance may have been overlooked, or that a typographical error may have occurred. The Editor and the Revision Committee will be grateful if readers will draw their attention to any such errors, and they will welcome suggestions regarding the subject matter or arrangement of the work from medical men or pharmacists.

Assistance has been obtained from several persons having special knowledge of and experience in the different parts of the work and on particular drugs, and the Council of the Pharmaceutical Society desire to record their indebtedness to all these helpers and particularly to the members of their laboratory and office staff, whose perseverance has made it possible to produce a completely revised edition in such a comparatively short time.

*December 1936*

## ABBREVIATIONS

The abbreviated titles of journals are those given in the *World List of Scientific Periodicals* (2nd Edn, 1934). When the reference is to a periodical of which two volumes are published during a year the number placed first indicates the first or second volume of the year followed by the year, and the last number refers to the page, thus, *Brit med J*, 1/1932, 250. When only one volume of a periodical is published each year, the reference gives the year and the page, thus, *Quart J Pharm*, 1934, 341. In other cases the volume number is given in italics in addition to the year and page, thus, *J biol Chem*, 1928, 17, 797.

$\alpha$ —optical rotation

*A O A C*—Methods of Analysis of the Association of Official Agricultural Chemists, Washington, 3rd Edn, 1930

*A R*—Reagent for Analytical Purposes

*Acta paediatr*, *Stockh*—Acta paediatrica

*Allen*—Allen's Commercial Organic Analysis 5th Edn, Vols I-VI edited by S S Sadtler, E C Lathrop and C A Mitchell, Vols VII-X edited by C A Mitchell (1924-1933)

*Amer J Cancer*—American Journal of Cancer

*Amer J Dis Child*—American Journal of Diseases of Children

*Amer J Hyg*—American Journal of Hygiene

*Amer J med Sci*—American Journal of Medical Sciences

*Amer J Obstet Gynec*—American Journal of Obstetrics and Gynecology

*Amer J Pharm*—American Journal of Pharmacy

*Amer J Physiol*—American Journal of Physiology

*Amer J Publ Hlth*—American Journal of Public Health

*Amer J Syph*—American Journal of Syphilis

*Amer J trop Med*—American Journal of Tropical Medicine

*Amer Perfum*—American Perfumer and Essential Oil Review

*Amer Rev Tuberc (Suppl)*—American Review of Tuberculosis (Supplement)

*Analyst*—Analyst

*Ann Eugen, Camb*—Annals of Eugenics

*Ann Falsif*—Annales des Falsifications

*Ann Hyg publ, Paris*—Annales d'hygiène publique et de médecine légale (industrielle et sociale)

*Ann Inst Pasteur*—Annales de l'Institut Pasteur

*Ann Surg*—Annals of Surgery

*Ann trop Med Parasit*—Annals of Tropical Medicine and Parasitology

*Apothekerzeitg, Berl*—Apothekerzeitung, Berlin

*Arch Derm Syph, N Y*—Archives of Dermatology and Syphilology

*Arch Dis Childh*—Archives of Disease in Childhood.

*Arch exp Path Pharmac*—Archiv für experimentelle Pathologie u Pharmakologie

*Arch int Pharmacodyn*—Archives internationales de pharmacodynamie et de thérapie

*Arch intern Med*—Archives of Internal Medicine

*Arch Kinderheilk*—Archiv für Kinderheilkunde

*Arch klin Chir*—Archiv für klinische Chirurgie

*Arch Méd Enf*—Archives de médecine des enfants

*Arch Pharm, Berl.*—Archiv der Pharmazie

*Arch Pharm Chem*—Archiv für Pharmaci og Chemi

*Arch Neurol Psychiat, Lond*—Archives of Neurology and Psychiatry

*Arch Radiol Electrother*—Archives of Radiology and Electrotherapy

*Ass méd*—Association médicale

*b p*—boiling-point

*B P '14*—British Pharmacopœia, 1914

*B P '32*—British Pharmacopœia, 1932

*B P Add*—Addendum, 1936, to the British Pharmacopœia, 1932

*B.P.C*—British Pharmaceutical Codex, 1934

*Barnett*—Preparation of Organic Compounds, by E de Barry Barnett, 2nd Edn, 1920.

*Ber. dtsh chem Ges*—Bericht der Deutschen Chemischen Gesellschaft

*Berl klin. Wschr*—Berliner klinische Wochenschrift

*Biochem. J.*—Biochemical Journal



- Biochem. Z.*—Biochemische Zeitschrift.  
*Boll. Ist. sieroter., Milano*—Bollettino dell'Istituto sieroterapico milanese  
*Brit. chem. Abstr.*—British Chemical Abstracts (A) Pure Chemistry. (B) Applied Chemistry.  
*Brit. colon. Drugg.*—British and Colonial Druggist (since 1915—British and Colonial Pharmacist).  
*Brit. colon. Pharm.*—British and Colonial Pharmacist  
*Brit. dent. J.*—British Dental Journal  
*Brit. J. Actino-Therap.*—British Journal of Actinotherapy and Physiotherapy  
*Brit. J. Biophys.*—British Journal of Biophysics  
*Brit. J. Child. Dis.*—British Journal of Children's Diseases  
*Brit. J. Derm.*—British Journal of Dermatology  
*Brit. J. exp. Path.*—British Journal of Experimental Pathology  
*Brit. J. phys. Med.*—British Journal of Physical Medicine  
*Brit. J. Radiol. (B.A.R.P. Sect.)*—British Journal of Radiology (British Association for the Advancement of Radiology and Physiotherapy Section), continued since 1927 as British Journal of Radiology, New Series  
*Brit. J. Radiol., N.S.*—British Journal of Radiology, New Series  
*Brit. J. Radiol. (Rontg. Soc. Sect.)*—British Journal of Radiology (Röntgen Society Section), continued since 1927 as British Journal of Radiology, New Series  
*Brit. J. Surg.*—British Journal of Surgery.  
*Brit. J. vener. Dis.*—British Journal of Venereal Diseases  
*Brit. med. J.*—British Medical Journal  
*Brit. med. J. Epit.*—British Medical Journal Epitome.  
*Brompton H.*—Pharmacopœia of the Hospital for Consumption and Diseases of the Chest, 11th Edn., 1928  
*Brooke*—Tropical Medicine, Hygiene and Parasitology, by Gilbert E. Brooke, 1920  
*Bruce and Dilling*—Bruce and Dilling's Materia Medica and Therapeutics, by W. J. Dilling, 14th Edn., 1933  
*Bull. Acad. Méd. Paris*—Bulletin de l'Académie de médecine  
*Bull. Dep. Agric. Can.*—Bulletin of the Department of Agriculture of the Dominion of Canada.  
*Bull. Féd. int. Pharm.*—Bulletin de la Fédération internationale pharmaceutique  
*Bull. Hyg.*—Bulletin of Hygiene  
*Bull. imp. Inst., Lond.*—Bulletin of the Imperial Institute  
*Bull. Inst. Pasteur*—Bulletin de l'Institut Pasteur.  
*Bull. Off. int. Hyg. publ.*—Bulletin mensuel de l'Office internationale d'hygiène publique.  
*Bull. Soc. chim. Fr.*—Bulletin, Société chimique de France.  
*Bull. Soc. méd. Hôp. Paris*—Bulletin et mémoires de la Société médicale des hôpitaux de Paris  
*Bull. tech. Mus., Sydney*—Bulletin of the Technological Museum, Sydney  
*C.H.W.*—Formulae of Chelsea Hospital for Women, 1927  
*C.L.T.H.*—Formulae of the Central London Throat, Nose and Ear Hospital, 3rd Edn., 1924  
*C.X.H.*—Charing Cross Hospital Pharmacopœia, 1922  
*Canad. Form.*—The Canadian Formulary, 1933.  
*Canad. med. Ass. J.*—Canadian Medical Association Journal  
*Canad. publ. Hlth. J.*—Canadian Public Health Journal  
*Chem. Abstr.*—Chemical Abstracts.  
*Chem. & Drugg.*—Chemist and Druggist  
*Chem. Ind. Rev.*—Chemistry and Industry Review  
*Chem. Z.*—Chemische Zeitschrift  
*Chininum*—Chininum Scriptioes Collectae, Bureau for increasing the use of Quinine, Amsterdam, 1925  
*Clin. J.*—Clinical Journal  
*cm.*—centimetre.  
*Colyer*—Colyer's Dental Surgery and Pathology, by Sir J. F. Colyer, 6th Edn., 1931, and earlier issues (previously Smale and Colyer's Diseases and Injuries of Teeth).  
*C.R. Acad. Sci., Paris*—Compte rendu hebdomadaire des séances de l'Académie des sciences  
*C.R. Soc. Biol. Paris*—Compte rendu hebdomadaire des séances et mémoires de la Société de biologie

- Cushny*—Text-book of Pharmacology and Therapeutics, by A. R. Cushny, 10th Edn., revised by C. W. Edmunds and J. A. Gunn (1934)
- [D]—Drugs or preparations coming within the scope of the Dangerous Drugs Acts, 1920, 1923, 1925 and 1932, and the Dangerous Drugs (Consolidation) Regulations, 1928.
- Dansk Tidsskr. Farm.*—*Dansk Tidsskrift for Farmaci*
- Dtsch. med. Wschr.*—*Deutsche medizinische Wochenschrift*
- Disp.*—Art of Dispensing, published by *The Chemist and Druggist*, London, 10th Edn., 1926
- Dixon*—Manual of Pharmacology, by the late W. E. Dixon, F.R.S., 7th Edn., 1929
- E. G. A.*—Pharmacopœia of the Elizabeth Garrett-Anderson Hospital, 1926
- Ec. Prod. India*—Economic Products of India
- Edinb. med. J.*—Edinburgh Medical Journal
- Emery*—Clinical Bacteriology and Hæmatology, by W. d'Este Emery, 6th Ed., 1921
- F. E. VIII.*—*Farmacopea Espanola* Octava Edición, 1930
- f. p.*—freezing-point
- Fr. Cx.*—*Codex Medicamentarius Gallicus*, *Pharmacopée Française* (1908)
- Fr. Cx. Supp. I to V*—Supplements I (1920) to V (1926) of the *Codex Medicamentarius Gallicus*
- Finnemore*—Essential Oils, their Chemistry and Technology, by H. Finnemore, 1926.
- g*—gramme
- G. H.*—Pharmacopœia of Guy's Hospital, 1916
- Gehe*—Gehe's Codex, 6th Edn., 1933
- Ghosh*—Treatise on Materia Medica and Therapeutics, by the late R. Ghosh, I.M.S. Edited by B. H. Deane, 12th Edn., 1930
- Glasg. med. J.*—Glasgow Medical Journal
- gr*—grain
- Gradwohl and Blaivas*—The Newer Methods of Blood and Urine Chemistry, by R. B. H. Gradwohl and A. J. Blaivas, 2nd Edn., 1920
- Gr. Orm. H.*—Pharmacopœia of the Hospital for Sick Children, Great Ormond Street, 1931
- Hager*—Handbuch der Pharmaceutischen Praxis, revised by G. Friedericks, G. Arends and H. Zörnig, 1925
- Hale-White*—Hale-White's Materia Medica, Pharmacy, Pharmacology and Therapeutics, revised by A. H. Douthwaite, 22nd Edn., 1935
- Hare*—Text-Book of Practical Therapeutics, by H. A. Hare, 21st Edn., 1930
- Helv. chim. Acta*—*Helvetica chimica acta*
- Hewlett and McIntosh*—A Manual of Bacteriology, 9th Edn., revised by R. T. Hewlett and J. McIntosh, 1932.
- Hoppe-Seyl. Z.*—Hoppe-Seyler's Zeitschrift für physiologische Chemie.
- Hospitalstüdende*—Hospitalstüdende
- Hutchison*—Food and Principles of Dietetics, by R. Hutchison and V. H. Mottram, 7th Edn., 1933.
- I. A.*—International Agreement, 1930
- I. V.*—iodine value.
- I. c. Add.*—Indian and Colonial Addendum (1900) to the B. P. 1898
- Indian J. med. Res.*—Indian Journal of Medical Research.
- Indian med. Gaz.*—Indian Medical Gazette.
- Indian med. Res. Mem.*—Indian Medical Research Memoirs
- Industr. Engng. Chem. (anal. Edn.)*—Industrial and Engineering Chemistry, (Analytical Edition)
- Int. Conf. trop. Amer.*—Proceedings of the International Conference on Health Problems in Tropical America, 1924, United Fruit Co., Boston
- Int. J. Leprosy*—International Journal of Leprosy
- Int. J. Med.*—International Journal of Medicine and Surgery, now included in Surgical Journal.
- J. R. Army med. Cps.*—Journal of the Royal Army Medical Corps
- J. R. nav. med. Serv.*—Journal of the Royal Naval Medical Service
- J. agric. Sci.*—Journal of Agricultural Science.
- J. Allergy*—Journal of Allergy.
- J. Amer. chem. Soc.*—Journal of the American Chemical Society.
- J. Amer. diet. Ass.*—Journal of the American Dietetic Association.
- J. Amer. med. Ass.*—Journal of the American Medical Association.

- J. Amer. pharm. Ass*—Journal of the American Pharmaceutical Association.  
*J. Ass. off. agric. Chem., Wash.*—Journal of the Association of Official Agricultural Chemists.  
*J. biol. Chem*—Journal of Biological Chemistry.  
*J. Cancer Res*—Journal of Cancer Research.  
*J. chem. Soc*—Journal of the Chemical Society.  
*J. chem. Soc. Abstr*—Journal of the Chemical Society Abstracts (continued since 1926 as British Chemical Abstracts).  
*J. clin. Invest.*—Journal of Clinical Investigation  
*J. clin. Res*—Journal of Clinical Research.  
*J. comp. Path.*—Journal of Comparative Pathology and Therapeutics  
*J. exp. Med.*—Journal of Experimental Medicine  
*J. Hyg., Camb*—Journal of Hygiene.  
*J. Immunol.*—Journal of Immunology  
*J. Indian med. Ass*—Journal of the Indian Medical Association  
*J. infect. Dis*—Journal of Infectious Diseases  
*J. Instn elect. Engrs*—Journal of the Institution of Electrical Engineers  
*J. Lab. clin. Med*—Journal of Laboratory and Clinical Medicine  
*J. Laryng.*—Journal of Laryngology (Rhinology) and Otology  
*J. ment. Sci.*—Journal of Mental Science.  
*J. Obstet. Gynaec.*—Journal of Obstetrics and Gynaecology of the British Empire  
*J. Path. Bact*—Journal of Pathology and Bacteriology  
*J. Pharm. Chim., Paris*—Journal de pharmacie et de chimie  
*J. Pharmacol*—Journal of Pharmacology and Experimental Therapeutics  
*J. Prat., Paris*—Journal des praticiens  
*J. Physiol*—Journal of Physiology  
*J. Röntgen Soc*—Journal of the Röntgen Society, continued from 1924 to 1927 as The British Journal of Radiology (Röntgen Society Section), and since 1927 as The British Journal of Radiology, New Series  
*J. State Med*—Journal of State Medicine  
*J. Soc. chem. Ind., Lond*—Journal of the Society of Chemical Industry  
*J. Suisse Pharm*—Journal suisse de pharmacie, now Schweizerische Apothekerzeitung  
*J. Text. Inst., Manch*—Journal of the Textile Institute, Manchester  
*J. trop. Med. (Hyg)*—Journal of Tropical Medicine and Hygiene  
*K.C.H*—King's College Hospital Pharmacopœia, 1934  
*Kenwood*—Public Health Laboratory Work, by H. R. Kenwood, 8th Edn, 1925  
*Klin. Wschr*—Klinische Wochenschrift  
*Knox*—Radiography and Radio-Therapeutics, by Robert Knox, 4th Edn, in 2 vols (Vol. II completed and edited by W. M. Levitt), 1923-32.  
*L.H.*—London Hospital Pharmacopœia, 1934  
*L.L.*—London Lock Hospitals Pharmacopœia  
*Lancet*—Lancet.  
*Leprosy Rev.*—Leprosy Review  
*m*—minim  
*ma*—milhampere  
*mp*—melting-point  
*M.R.C.*—Medical Research Council  
*M.R.I.*—Manchester Royal Infirmary Pharmacopœia  
*May*—Chemistry of Synthetic Drugs, by Percy May, 3rd Edn, 1921  
*Med. Annu*—Medical Annual  
*Med. J. Aust*—Medical Journal of Australia  
*Med. J. Rec.*—Medical Journal and Record  
*Med. Klinik*—Medizinische Klinik  
*Med. Offr*—Medical Officer.  
*Med. Pr.*—The Medical Press and Circular  
*Med. Rec., N.Y.*—Medical Record  
*Medicine, Baltimore*—Medicine, Baltimore  
*Mem. Univ. Calif*—Memoirs of the University of California  
*Merck*—E. Merck's Annual Report of recent advances in Pharmaceutical Chemistry and Therapeutics  
*Merck's Index*—Merck's Index, 5th Edn, 1927  
*Mfg. Chem*—Manufacturing Chemist  
*mg*—milligramme  
*ml*—millilitre.

- Mod Tech in Treatment*—Modern Technique in Treatment, Vols 1-4, 1925-28  
*The Lancet*, London
- Muir and Ritchie*—Manual of Bacteriology, by R Muir and J Ritchie, 9th Edn, 1932.
- Munch med. Wschr*—Munchener medizinische Wochenschrift
- Murrell*—What to do in Cases of Poisoning, by William Murrell, 13th Edn, 1925, revised by P. Hamill
- Mid H.*—Middlesex Hospital Pharmacopœia, 1927
- n*—refractive index
- N F. VI*—National Formulary of Unofficial Preparations, issued by the American Pharmaceutical Association, 6th Edn, 1936
- N H.*—Prescription Formulæ for Use in Naval Hospitals, 1930
- N I F*—National Formulary for National Health Insurance Purposes, issued by the British Medical Association, 2nd Edn, 1933
- N N R*—New and Non-official Remedies, 1936, issued by the American Medical Association
- Nature, Lond*—Nature, London
- Naturwissenschaften*—Naturwissenschaften
- Nav. med. Bull., Wash*—Naval Medical Bulletin, Washington
- New Engl J Med.*—New England Journal of Medicine
- Nutr Abstr Rev*—Nutrition Abstracts and Reviews
- N Y St J Med*—New York State Journal of Medicine
- [*P1*]—Part 1 of the Poisons List
- [*P2*]—Part 2 of the Poisons List.
- P E H C*—Pharmacopœia of the Princess Elizabeth of York Hospital for Children (formerly the East London Hospital), 1933
- P G VI.*—German Pharmacopœia, 1926
- P. J F*—Pharmaceutical Journal Formulary
- P L*—Pharmacopœia Londinensis, 1851.
- P M C E*—Select Parliamentary Committee on Proprietary Medicines Enquiry, 1912-13
- P Argent II*—Pharmacopœia of the Argentine Republic, 2nd Edn, 1919
- P Austr*—Austrian Pharmacopœia, 1906
- P Belg IV*—Belgian Pharmacopœia, 1930
- P Dan*—Danish Pharmacopœia, 1933
- P Helv V*—Swiss Pharmacopœia 1933
- P Ital V*—Italian Pharmacopœia, 1929
- P Jap IV*—Japanese Pharmacopœia, 1921 (English translation, 1922)
- P Ned I*—Netherlands Pharmacopœia, 1926
- P Russ*—Russian Pharmacopœia, 1926
- P Svec*—Swedish Pharmacopœia, 1925
- Paris méd*—Paris médical La semaine du clinicien
- Perfum essent Oil Rec*—Perfumery and Essential Oil Record
- Ph Form*—Pharmaceutical Formulas, 9th Edn, Second Reprint, 1921, by Peter MacEwan, and 10th Edn, Vol 1, 1929, revised by S W Woolley and G P Forrester, Vol II, 1934, revised by G P Forrester, *The Chemist and Druggist*, London
- Pharm J*—Pharmaceutical Journal
- Pharm Weekbl*—Pharmaceutisch Weekblad voor Nederland
- Pharm Ztg, Berl*—Pharmazeutische Zeitung
- Philipp J Sci*—Philippine Journal of Science
- Physiol Rev*—Physiological Reviews
- Pr méd*—Presse médicale
- Practitioner*—Practitioner
- Prescriber*—Prescriber.
- Proc Mayo Clin*—Proceedings of Staff Meetings of the Mayo Clinic
- Proc nat Acad Sci*—Proceedings of the National Academy of Science
- Proc roy Soc*—Proceedings of the Royal Society
- Proc roy Soc Edinb*—Proceedings of the Royal Society of Edinburgh
- Proc R Soc Med*—Proceedings of the Royal Society of Medicine
- Proc Soc exp Biol, N Y*—Proceedings of the Society for Experimental Biology and Medicine
- Publ Hlth, Lond*—Public Health.
- Publ Hlth Rep, Wash*—Public Health Reports, issued by the United States Public Health Service

- Quart. Bull. Hlth Org L. o. N.*—Quarterly Bulletin of the Health Organisation of the League of Nations.
- Quart. J. exp. Physiol*—Quarterly Journal of Experimental Physiology
- Quart. J. Med.*—Quarterly Journal of Medicine.
- Quart. J. Pharm.*—Quarterly Journal of Pharmacy and Pharmacology.
- Quart J Physiol.*—Quarterly Journal of Experimental Physiology
- R.D.H.*—Pharmacopœia of the Royal Dental Hospital, London, 1926
- R.F.H.*—Pharmacopœia of the Royal Free Hospital, London, 1922.
- R.I.*—Refractive Index.
- R.I. Edinb.*—Pharmacopœia of the Royal Infirmary, Edinburgh, 1935.
- R.L.O.H.*—Pharmacopœia of the Royal London Ophthalmic Hospital (Moorfields Eye Hospital), 1929
- R.N.H.*—Pharmacopœia of the Royal Northern Group of Hospitals, 1930
- R.V.I.*—Pharmacopœia of the Royal Victoria Infirmary, Newcastle-on-Tyne
- Rem*—Remington's Practice of Pharmacy, 7th Edn., 1926
- Rep Brit. Emp Cancer Campgn*—Report of the British Empire Cancer Campaign
- Rep Cancer Res Fd*—Report of the Imperial Cancer Research Fund
- Rep. Inst. med. Res. F.M.S.*—Report of the Institute for Medical Research, Federated Malay States
- Rep med Offr Minist Hlth, Lond*—Report of the Chief Medical Officer, the Ministry of Health
- Rep. med Res. Coun, Lond.*—Report of the Medical Research Council
- Rep. metrop. Asylums Bd*—Report of the Metropolitan Asylums Board
- Rep metrop. Wat. Bd.*—Report of the Metropolitan Water Board
- Rep publ. Hlth med. Subj., Lond*—Report on Public Health and Medical Subjects, Ministry of Health
- Retail Chem*—Retail Chemist.
- 81j—First Schedule to the Poisons Rules, 1935 Other Schedules are indicated by the corresponding numerical suffix.
- S.R.A., F.D., No. 2, Rev 4*—Service and Regulatory Announcements, Food and Drug No 2 (Fourth Revision), issued by the United States Department of Agriculture, Food and Drug Administration, August 1933
- S.R. & O*—Statutory Rules and Orders, His Majesty's Stationery Office, London
- S.V.*—saponification value
- St B.H.*—Pharmacopœia of St. Bartholomew's Hospital, 1921
- St G.H.*—Pharmacopœia of St. George's Hospital, 1927
- St J.H.*—Pharmacopœia of St. John's Hospital for Skin Diseases, 1926
- St M.H.*—Pharmacopœia of St. Mary's Hospital, 1934
- St Mark's H.*—Pharmacopœia of St. Mark's Hospital for Diseases of the Rectum and Colon, 1935
- St T.H.*—Pharmacopœia of St. Thomas' Hospital, 1931
- S Afr med J*—South African Medical Journal
- Schmidt*—Ausführliches Lehrbuch der Pharmaceutischen Chemie, Vol I (Inorganic), Vol II (Organic), Part I (1922), Part II (1923), by Ernst Schmidt
- Schweiz ApothZtg*—Schweizerische Apothekerzeitung
- Schweiz med Wschr.*—Schweizerische medizinische Wochenschrift
- Sci Rep Cancer Res. Fd, Lond*—Scientific Reports on the Investigations of the Imperial Cancer Research Fund
- Secret Remedies*—Secret Remedies, What they Cost and What they Contain—British Medical Association (1909), also "More Secret Remedies" (1912)
- Seidell*—Solubilities of Inorganic and Organic Substances, 2nd Edn, 1920
- Soddy*—Interpretation of Radium, by F. Soddy, 4th Edn, 1920
- Sp gr.*—specific gravity.
- Spec. Rep. Food Invest. Bd, Lond*—Special Report, Food Investigation Board, Department of Scientific and Industrial Research
- Spec Rep Ser med. Res. Comm.*—National Health Insurance, Medical Research Committee, Special Report Series.
- Spec. Rep Ser. med Res Coun., Lond*—Special Report Series, Medical Research Council, London.
- Stutt*—Practical Bacteriology, Blood Work and Animal Parasitology, by E. R. Stutt, 8th Edn, 1927
- Surg Gynec. Obstet.*—Surgery, Gynecology and Obstetrics
- Svensk farm Tidskr*—Svensk farmaceutisk Tidskrift.
- T.H.*—Pharmacopœia of the Golden Square Throat, Nose and Ear Hospital, 1935
- Thorpe*—Dictionary of Applied Chemistry, 7 vols, edited by Sir E. Thorpe

- (Vols. VI and VII with assistance of H. F. Morley), 1921-7, and Supplement, 3 vols., by J. F. Thorpe and M. A. Whiteley, 1934-6.
- Topley and Wilson*—The Principles of Bacteriology and Immunity, by W. W. C. Topley and G. S. Wilson, 1929.
- Trans. Brit. Soc. dent. Surg.*—Transactions of the British Society of Dental Surgeons
- Trans. R. Soc. trop. Med. Hyg.*—Transactions of the Royal Society of Tropical Medicine and Hygiene
- Trop. Dis. Bull.*—Tropical Diseases Bulletin
- U. C. H.*—Pharmacopœia of University College Hospital, 1933
- U. F. C.* '25—Fourteenth Annual Report, United Fruit Co., Medical Dept., 1925
- U. S. D.*—United States Dispensatory, 21st Edn., 1926
- U. S. P. XI*—Pharmacopœia of the United States, 1935
- Urol. cutan. Rev.*—Urologic and Cutaneous Review
- V. H. C.*—Pharmacopœia of the Victoria Hospital for Children (Chelsea), 1920
- v/v*—volume in volume, *w/w*—volume in weight.
- Vet. J.*—Veterinary Journal
- Vic. Park*—City of London Hospital for Diseases of the Heart and Lungs, Victoria Park, E 2, 1926
- W.*—Pharmacopœia of the Hospital for Women (Soho Square), 1927
- w/v*—weight in volume, *w/w*—weight in weight.
- W. H.*—Pharmacopœia of Westminster Hospital, 1934.
- Ward and Smith*—Recent Advances in Radium, by W. Roy Ward and A. J. Durden Smith, 1933
- Wenyon*—Protozoology, by C. M. Wenyon, 2 vols., 1926
- Wien. klin. Wschr.*—Wiener klinische Wochenschrift
- Wynter Blyth*—Foods: Their Composition and Analysis, by the late A. Wynter Blyth and M. Wynter Blyth, 7th Edn., revised by H. E. Cox, 1927
- Yearb. Pharm.*—The Yearbook of Pharmacy (since 1928 The Quarterly Journal of Pharmacy and Pharmacology).
- Z. anal. Chem.*—Zeitschrift für analytische Chemie.
- Z. angew. Chem.*—Zeitschrift für angewandte Chemie und Zentralblatt für technische Chemie (Since 1932, continued as *Angewandte Chemie*)
- Z. Immunforsch.*—Zeitschrift für Immunitätsforschung und experimentelle Therapie
- Z. Hyg. InfektKr.*—Zeitschrift für Hygiene und Infektionskrankheiten
- Z. klin. med.*—Zeitschrift für klinische Medizin.

## PERCENTAGE AND GRAINS PER FLUID OUNCE EQUIVALENTS

Where **Percentage Solutions** are mentioned, it is intended that 100 millilitres shall contain *n* grammes or that 100 grain-measures of the finished solution shall contain *n* grains of the substance, e.g., a 50 per cent. solution of Cocaine Hydrochloride will contain 50 g. in 100 ml. or 50 grains in 100 grain-measures

%	Grains per fluid ounce	%	Grains per fluid ounce	%	Grains per fluid ounce
10.0	43.75	4.5	19.7	1.4	6.1
9.5	41.56	4.0	17.5	1.3	5.7
9.0	39.4	3.5	15.3	1.2	5.25
8.5	37.2	3.0	13.1	1.1	4.8
8.0	35.0	2.5	10.95	1.0	4.4
7.5	32.8	2.0	8.75	0.9	3.95
7.0	30.6	1.9	8.3	0.8	3.5
6.5	28.45	1.8	7.9	0.7	3.05
6.0	26.25	1.7	7.45	0.6	2.6
5.5	24.05	1.6	7.0	0.5	2.2
5.0	21.9	1.5	6.55	0.4	1.75

# WEIGHTS AND MEASURES APPROXIMATE EQUIVALENTS WEIGHTS. IMPERIAL TO METRIC

grain	gramme	grain	gramme	grains	grammes
$\frac{1}{1000}$ = 0.00065		$\frac{1}{4}$ = 0.016		15 = 1.0	
$\frac{1}{500}$ = 0.0003		$\frac{1}{2}$ = 0.02		20 = 1.2	
$\frac{1}{100}$ = 0.0006		$\frac{3}{4}$ = 0.03		30 = 2.0	
$\frac{1}{80}$ = 0.001		$\frac{1}{2}$ = 0.05		45 = 3.0	
$\frac{1}{60}$ = 0.0013		1 = 0.06		60 = 4.0	
$\frac{1}{40}$ = 0.0015		grains	gramme	90 = 6.0	
$\frac{1}{32}$ = 0.002		$1\frac{1}{2}$ = 0.1		120 = 8.0	
$\frac{1}{24}$ = 0.0025		2 = 0.12		150 = 10.0	
$\frac{1}{20}$ = 0.003		3 = 0.2		180 = 12.0	
$\frac{1}{16}$ = 0.004		4 = 0.25		$\frac{1}{2}$ ounce	
$\frac{1}{12}$ = 0.005		5 = 0.3		(av.) = 15.0	
$\frac{1}{10}$ = 0.006		6 = 0.4		1 = 30.0	
$\frac{1}{8}$ = 0.008		8 = 0.5		(or nearer 28.35)	
$\frac{1}{6}$ = 0.01		10 = 0.6		1 pound	
$\frac{1}{5}$ = 0.012		12 = 0.8		= 453.59	

## WEIGHTS. METRIC TO IMPERIAL.

1 kilogramme	= 2 lb.	$3\frac{1}{2}$ oz
500 grammes	= 1 "	$1\frac{1}{2}$ "
100 "	= $3\frac{1}{2}$ oz	
25 "	= $\frac{7}{8}$ "	
10 "	= $\frac{1}{2}$ "	
1 "	= 15.43 grains	
$\frac{1}{2}$ " or 500 milligrammes	= 7.7 "	

## MEASURES. IMPERIAL TO METRIC

minim	ml.	minims	ml	fluid oz	ml
$\frac{1}{2}$ = 0.03		15 = 1.0		1 = 30.0	
1 = 0.06		20 = 1.2		fluid ozs	
minims		25 = 1.5		2 = 60.0	
2 = 0.12		30 = 2.0		4 = 115.0	
3 = 0.2		40 = 2.5		5 = 140.0	
4 = 0.25		45 = 3.0		6 = 170.0	
5 = 0.30		60 = 4.0		8 = 230.0	
6 = 0.4		90 = 6.0		10 = 280.0	
8 = 0.5		120 = 8.0		20 = 568.0	
10 = 0.6		240 = 15.0		gallon	litres
12 = 0.8				1 = 4.536	

## MEASURES. METRIC TO IMPERIAL

1 ml.	= 15 (nearer 17) minims
1 litre	= 1 pint 15 fl. oz approx

## MEASURES OF LENGTH.

1 micromillimetre	= $\frac{1}{1000000}$ millimetre, usually represented by $m\mu$
1 micron	= $\frac{1}{1000}$ millimetre, or 1 micrometre " " $\mu$
1 millimetre	= 0.03937 inch.
1 centimetre	= 0.3937 inch
1 decimetre	= 3.937 inches.
1 metre	= 39.370113 inches or 1 yard 3.37 inches nearly.

## MISCELLANEOUS EQUIVALENTS

1 minim = the volume at 16 °C of 0.9114583 grain of water

1 fluid drachm = the volume at 16 °C of 54.6875 grains of water

1 fluid ounce = the volume at 16 °C of 437.5 grains of water

109.7143 minims (taken as 110 minims) = the volume at 16 °C of 100 grains of water

1 grain per gallon =  $\frac{100}{7}$  parts per million

1 part per million =  $\frac{7}{100}$  grains per gallon

1 pound = 7000 grains, 10% w/v = 700 grains per lb

$\frac{1}{100}$  grain per lb = approx 1.4 parts per million

A gallon of Water weighs 10 pounds

A "Corbyn" = 40 ounces fluid (1 quart)

A "Winchester" quart = 80 ounces fluid ( $\frac{1}{2}$  gallon)

## PROPORTIONAL DOSES ACCORDING TO AGE

The following are some of the methods that have been proposed for calculating the dose for a child from that for an adult

## Gaubius' Method

Under	1 year will require	$\frac{1}{12}$	the adult dose
" 2 years	" "	$\frac{1}{6}$	" " "
" 3	" "	$\frac{1}{4}$	" " "
" 4	" "	$\frac{1}{3}$	" " "
" 7	" "	$\frac{1}{2}$	" " "
" 14	" "	$\frac{2}{3}$	" " "
" 20	" "	$\frac{3}{4}$	" " "
From 21 to 60 years	will require	the full adult dose	

## Young's Formula.

$\frac{\text{Age}}{\text{Age} + 12}$  Thus for 8 years, the dose required is  $\frac{8}{8 + 12} = \frac{2}{5}$  of the adult dose. The formula applies only to children under 12.

**Dilling's Formula.** This method represents an attempt to correlate dose with body weight. Dilling states that the fraction  $\frac{\text{age}}{20}$  approximates closely to the weight curve, between the ages of 4 and 20.

## Clark's Formula.

$\frac{\text{Body weight in lb}}{150}$

## Fried's Formula.

For infants,  $\frac{\text{age in months}}{150}$

*Dosage for the aged.* Above the age of 60, an inverse gradation must be observed. The following are the fractions suggested (Dixon's *Manual of Pharmacology*, 8th Edn, revised by W. A. M. Smart, 1936) —

Aged 60 to 70.	$\frac{2}{3}$	the usual adult dose
" 70 to 80	$\frac{1}{2}$	" " "
" 80 to 90	$\frac{1}{3}$	" " "
Over 90	$\frac{1}{4}$	" " "



## CALCULATION OF A DOSE FOR MAN FROM KNOWN DOSE FOR AN ANIMAL

The rate of catabolism of an animal is not proportional to size or weight but approximately to the body surface. Surfaces of solids of the same shape are proportional to the two-thirds power of their volumes (*i.e.*, the cube root of the square of the volumes). Since the specific gravity of animals varies only slightly, their body surface is a function of the two-thirds power of their weight. This relation is expressed by Meeh's Formula,  $S = k(W)^{\frac{2}{3}}$ , where  $S$  is the surface in square centimetres,  $W$  is the weight in grammes, and  $k$  is a factor which is nearly constant for all animals of the same shape.

(Rubner gives the following values for  $k$ . Man, 12.3; Dog, 10.3—11.2; Rabbit, 12.0—12.9; Cat, 9.9; Guinea Pig, 10.5.)

*A formula for calculating the dose for man* This assumes that  $k$ , the factor, is the same for man and animals, and is approximate only, as the values actually differ somewhat.

If the dose for man and the animal should be proportional to their rates of catabolism, *i.e.*, to their body surface, then.

$$\frac{DM}{DA} = \frac{SM}{SA} = \frac{\kappa(M)^{\frac{2}{3}}}{\kappa(A)^{\frac{2}{3}}}$$

$DM$  = Dose for man in g.

$DA$  = Dose for adult test animal in

$\frac{g}{g}$

$SM$  = Body surface of man

$SA$  = Body surface of animal

$M$  = Wt. of man in g

$A$  = Wt. of test animal in g

$$\text{Hence } DM = \frac{M}{(A)^{\frac{2}{3}}} \times DA = \frac{1590 \times DA}{(A)^{\frac{2}{3}}}$$

for a 10-stone (63.5 kilo) man.

Thus, a dose of 1 g per kilo for an animal is equivalent to 15.9 g., not 63.5 g., for a 10-stone man.

No exact method of calculating the corresponding dose for man from that of an animal is known. The figure obtained by the above formula is useful as a guide, but allowance must still be made for the fact that man may be more sensitive to the drug than the animal.

## TRANSPOSITION TABLE OF DOSES STATED FOR MAN IN MG. PER KILO TO MAN'S WEIGHT

**Mg. per kilo.**

1	=	1 grain (0.065 g.)	for a 10-stone (63.5 kilo) man
5	=	5 „ (0.32 g.)	„ „ „ „
10	=	10 „ (0.64 g.)	„ „ „ „
50	=	50 „ (3.20 g.)	„ „ „ „

As 5 mg. per kilo more nearly = 4.9 grains (0.318 g.) per 10-stone man, the above figures contain a 2% error in excess

## THERMOMETRIC EQUIVALENTS

°C.	°F.	°C.	°F.	°C.	°F.	°C.	°F.	°C.	°F.	°C.	°F.
—	—	9	48 2	62	143 6	117	242 6	172	341 6	227	440 6
40	40 0	10	50 0	63	145 4	118	244 4	173	343 4	228	442 4
39	38 2	11	51 8	64	147 2	119	246 2	174	345 2	229	444 2
38	36 4	12	53 6	65	149 0	120	248 0	175	347 0	230	446 0
37	34 6	13	55 4	66	150 8	121	249 8	176	348 8	231	447 8
36	32 8	14	57 2	67	152 6	122	251 6	177	350 6	232	449 6
35	31 0	15	59 0	68	154 4	123	253 4	178	352 4	233	451 4
34	29 2	16	60 8	69	156 2	124	255 2	179	354 2	234	453 2
33	27 4	17	62 6	70	158 0	125	257 0	180	356 0	235	455 0
32	25 6	18	64 4	71	159 8	126	258 8	181	357 8	236	456 8
31	23 8	19	66 2	72	161 6	127	260 6	182	359 6	237	458 6
30	22 0	20	68 0	73	163 4	128	262 4	183	361 4	238	460 4
29	20 2	21	69 8	74	165 2	129	264 2	184	363 2	239	462 2
28	18 4	22	71 6	75	167 0	130	266 0	185	365 0	240	464 0
27	16 6	23	73 4	76	168 8	131	267 8	186	366 8	241	465 8
26	14 8	24	75 2	77	170 6	132	269 6	187	368 6	242	467 6
25	13 0	25	77 0	78	172 4	133	271 4	188	370 4	243	469 4
24	11 2	26	78 8	79	174 2	134	273 2	189	372 2	244	471 2
23	9 4	27	80 6	80	176 0	135	275 0	190	374 0	245	473 0
22	7 6	28	82 4	81	177 8	136	276 8	191	375 8	246	474 8
21	5 8	29	84 2	82	179 6	137	278 6	192	377 6	247	476 6
20	4 0	30	86 0	83	181 4	138	280 4	193	379 4	248	478 4
19	2 2	31	87 8	84	183 2	139	282 2	194	381 2	249	480 2
18	0 4	32	89 6	85	185 0	140	284 0	195	383 0	250	482 0
17 778	0 0	33	91 4	86	186 8	141	285 8	196	384 8	251	483 8
—	—	34	93 2	87	188 6	142	287 6	197	386 6	252	485 6
17	1 4	35	95 0	88	190 4	143	289 4	198	388 4	253	487 4
16	3 2	36	96 8	89	192 2	144	291 2	199	390 2	254	489 2
15	5 0	37	98 6	90	194 0	145	293 0	200	392 0	255	491 0
14	6 8	37 5	99 5	91	195 8	146	294 8	201	393 8	256	492 8
13	8 6	38	100 4	92	197 6	147	296 6	202	395 6	257	494 6
12	10 4	39	102 2	93	199 4	148	298 4	203	397 4	258	496 4
11	12 2	39 5	103 1	94	201 2	149	300 2	204	399 2	259	498 2
10	14 0	40	104 0	95	203 0	150	302 0	205	401 0	260	500 0
9	15 8	41	105 8	96	204 8	151	303 8	206	402 8	261	501 8
8	17 6	42	107 6	97	206 6	152	305 6	207	404 6	262	503 6
7	19 4	43	109 4	98	208 4	153	307 4	208	406 4	263	505 4
6	21 2	44	111 2	99	210 2	154	309 2	209	408 2	264	507 2
5	23 0	45	113 0	100	212 0	155	311 0	210	410 0	265	509 0
4	24 8	46	114 8	101	213 8	156	312 8	211	411 8	266	510 8
3	26 6	47	116 6	102	215 6	157	314 6	212	413 6	267	512 6
2	28 4	48	118 4	103	217 4	158	316 4	213	415 4	268	514 4
1	30 2	49	120 2	104	219 2	159	318 2	214	417 2	269	516 2
0	32 0	50	122 0	105	221 0	160	320 0	215	419 0	270	518 0
+	+	51	123 8	106	222 8	161	321 8	216	420 8	271	519 8
1	33 8	52	125 6	107	224 6	162	323 6	217	422 6	272	521 6
2	35 6	53	127 4	108	226 4	163	325 4	218	424 4	273	523 4
3	37 4	54	129 2	109	228 2	164	327 2	219	426 2	274	525 2
4	39 2	55	131 0	110	230 0	165	329 0	220	428 0	275	527 0
5	41 0	56	132 8	111	231 8	166	330 8	221	429 8		
6	42 8	57	134 6	112	233 6	167	332 6	222	431 6		
7	44 6	58	136 4	113	235 4	168	334 4	223	433 4		
8	46 4	59	138 2	114	237 2	169	336 2	224	435 2		
		60	140 0	115	239 0	170	338 0	225	437 0		
		61	141 8	116	240 8	171	339 8	226	438 8		

\* Clinical Limits.

The Réaumur scale (with zero at freezing-point of water and the boiling-point of water being 80°) is now little used.

To convert C. into F. multiply by  $\frac{9}{5}$  and add 32. To transpose F. into C. subtract 32 and multiply by  $\frac{5}{9}$ . To convert C. into R. multiply by  $\frac{4}{5}$ . To convert R. into C. multiply by  $\frac{5}{4}$ . To convert F. into R. subtract 32 and multiply by  $\frac{4}{9}$ . To convert R. into F. multiply by  $\frac{9}{4}$  and add 32.

## INTERNATIONAL ATOMIC WEIGHTS

Element	Sym- bol	Atomic Weight	Element	Sym- bol	Atomic Weight
Aluminium	Al	26.97	Molybdenum	Mo	96.0
Antimony	Sb	121.76	Neodymium	Nd	144.27
Argon	A	39.944	Neon	Ne	20.183
Arsenic	As	74.91	Nickel	Ni	58.69
Barium	Ba	137.36	Nitrogen	N	14.008
Beryllium	Be	9.02	Osmium	Os	191.5
Bismuth	Bi	209.00	Oxygen	O	16.0000
Boron	B	10.82	Palladium	Pd	106.7
Bromine	Br	79.916	Phosphorus	P	31.02
Cadmium	Cd	112.41	Platinum	Pt	195.23
Calcium	Ca	40.08	Potassium	K	39.096
Carbon	C	12.00	Praseodymium	Pr	140.92
Cerium	Ce	140.13	Radium	Ra	225.97
Cesium	Cs	132.91	Radon	Rn	222.00
Chlorine	Cl	35.457	Rhenium	Re	186.31
Chromium	Cr	52.01	Rhodium	Rh	102.91
Cobalt	Co	58.94	Rubidium	Rb	85.44
Columbium	Cb	92.91	Ruthenium	Ru	101.7
Copper	Cu	63.57	Samarium	Sm	150.43
Dysprosium	Dy	162.46	Scandium	Sc	45.10
Erbium	Er	167.64	Selenium	Se	78.96
Europium	Eu	152.0	Silicon	Si	28.06
Fluorine	F	19.00	Silver	Ag	107.8870
Gadolinium	Gd	157.3	Sodium	Na	22.99
Gallium	Ga	69.72	Strontium	Sr	87.63
Germanium	Ge	72.60	Sulphur	S	32.06
Gold	Au	197.2	Tantalum	Ta	181.4
Hafnium	Hf	178.6	Tellurium	Te	127.61
Helium	He	4.002	Terbium	Tb	159.2
Holmium	Ho	163.5	Thallium	Tl	204.39
Hydrogen	H	1.0078	Thorium	Th	232.12
Indium	In	114.76	Thulium	Tm	169.4
Iodine	I	126.92	Tin	Sn	118.70
Iridium	Ir	193.1	Titanium	Ti	47.90
Iron	Fe	55.84	Tungsten	W	184.0
Krypton	Kr	83.7	Uranium	U	238.14
Lanthanum	La	138.92	Vanadium	V	50.95
Lead	Pb	207.22	Xenon	Xe	131.3
Lithium	Li	6.940	Ytterbium	Yb	173.04
Lutecium	Lu	175.0	Yttrium	Y	88.92
Magnesium	Mg	24.32	Zinc	Zn	65.38
Manganese	Mn	54.93	Zirconium	Zr	91.22
Mercury	Hg	200.61			



*The Editor would welcome any suggestions regarding the subject matter or arrangement of the work, from Medical Men, Pharmacists, or Analysts*

## ACACIA

*B P*, *U S P XI*, *Fr Cx*, *P Belg IV*, *P Ital V*, *F F VIII*,  
*P Helv V*, *P Dan*

*Syn* ACACIÆ GUMMI, GOMME ARABIQUE, GOMME DU SÉNÉGAL.

A gummy exudate from *A senegal* Willd (Leguminosæ), and other species, either colourless or with yellowish tint

The gum consists of a mixture of Ca, Mg and K arabinates

**Soluble** almost completely in water, insoluble in alcohol

**Incompatibles.** Alcohol, mineral acids, borax, ferric salts, oxalic acid and most lead salts. Bismuth carbonate should not be suspended with acacia mucilage, tragacanth is better

**Uses.** For intravenous injection to raise blood pressure after loss of blood, *e g*, from a wound of the femoral artery. Many such cases could be saved if the blood pressure could be kept up for 24 hours or so. The solution has the same viscosity as the blood and a content of colloids with osmotic pressure equal to that of the blood, hence after its injection there is little tendency for water to pass into the tissues. Large quantities may be used. In surgical shock the injection has been found of great value. The increase in blood volume caused, enables the heart to send on a large volume. When the total volume of blood is deficient the tissues suffer from want of oxygen though the blood may be of normal constitution. Normal saline was first proposed, but it disappears from the circulation in 20 to 30 minutes, a colloid with an osmotic pressure equal to that of the blood colloids must be added. Solutions of 5%, or over will restore permanently the low arterial pressure due to loss of blood.

Powdered acacia is used as an **emulsifying agent** for oils, the usual proportion being about 1 of gum to 4 of a fixed oil or 2 of a volatile oil. Less suffices in some cases. For its use as a pill excipient, *vide* *Pilule*.

**BURNS.** The secondary shock of burns is best treated by intravenous injection of 6% gum saline solution—normal saline or dextrose-saline will do more harm than good—W. C. Wilson, *Practitioner*, 1/1936, 398.

**DIABETIC COMA.** Desperate cases recovered with large quantities of fluid intravenously—hypertonic saline and acacia solution (7%)—R. D. Lawrence, *Brit med J*, 1/1930, 690.

**OBSTETRIC SHOCK** treated with definite benefit. Many lives saved by early use. Should be employed more extensively—L. M. Randall, *Amer med Ass*, 11/1929, 847.

**Injectio Sodii Chloridi et Acaciæ** (*B P*) Acacia 60 g, sodium chloride 9 g, freshly prepared distilled water to 1000 ml. The solution is autoclaved at 121° to 122° for one hour, cooled, filtered and again autoclaved.

**Solutio Salina cum Acacia** (*U C H*) has 0.91% w/v of sodium chloride

**Serum Colloidale Completum.** *Syn* SUERO COLOIDAL COMPLETO (*F F VIII*)

Acacia 70 g, sodium chloride 8 g, potassium chloride 0.2 g, calcium chloride 2 g, magnesium chloride 0.1 g, sodium carbonate 1.2 g, distilled water sufficient quantity to 1000 ml. Sterilise for 30 minutes at 115°.

**Sterules Acaciæ** (*Martindale, London*). The contents of one Sterule diluted to 250 ml. form a 7% solution of acacia in normal saline

**Mucilago Acaciæ** (*B P*) Acacia 4, washed to remove any adherent dust, dissolved in chloroform water 6 This quantity measures about 8½.

**Mucilago Acaciæ** (*U.S.P. XI*) Average dose—¼ ounce (15 ml)

Acacia 35% w/v and sodium benzoate 1% in water

**Pulvis Acaciæ Compositus.** Acacia 1, tragacanth 1 A useful pill excipient

**Syrupus Acaciæ** (*B.P.C.*).

**Dose.**—1 to 4 drachms (4 to 16 ml) Mucilage of acacia 1, syrup 3. A demulcent for use in cough mixtures Must be freshly prepared.

**Potion Gommeuse** (*Fr. Cx*) Acacia powder 1, syrup 3, orange flower water 1, water 10, parts by weight

**Gummi Arabicum Desenzymatum** (*P. Helv. V*) is obtained by evaporating the mucilage, drying and powdering the residue, the oxydases are thus destroyed

**Gummi Indici.** *Syn* GHATTI GUM From *Anogeissus latifolia* (Combretaceæ) Indian gum is used technically for the same purposes as acacia. **Mucilago Gummi Indici**, 1 to 3 of water, is used in place of mucilage of acacia in India and the Eastern Colonies.

**Acaciæ Cortex** (*B.P.C.*) The dried bark of *A. arabica* (Babul bark) and *A. decurrens* (Wattle bark) (Leguminosæ) **Decoctum Acaciæ Corticis** 6%, dose—½ to 2 fluid ounces; used occasionally as astringent internally or in gargles

## ACETANILIDUM

*B.P.C., P. Helv. V, U.S.P. XI, P. Dan., etc*

$C_6H_5NH \cdot CO \cdot CH_3 = 135.1$

*Syn* ANILFEBRIN, PHENYLACETAMIDE

[P1] "Acetanilide, alkyl acetanilides"

[S3] "Acetanilide, alkyl acetanilides—in substances not being preparations for the treatment of human ailments"

**Dose**—2 to 5 grains (0.12 to 0.3 g). Larger doses are sometimes given, but idiosyncrasy may exist. *P. Helv. V* has maximum daily dose 15 gr. *U.S.P. XI* average dose 3 gr. May be given in cachets or suspended by compound tragacanth powder

Prepared by the action of glacial acetic acid on aniline. In small white odourless glittering crystals which produce a burning sensation on the tongue.

**Soluble** 1 in 210 of water, 1 in 18 of boiling water, slightly in glycerin, 1 in 3.5 of alcohol, easily in chloroform, benzene and ether.

**Antidotes.** Empty stomach by stomach tube or emetic. Keep patient lying down and warm. Give aromatic spirit of ammonia, 1 dr., in 4 oz. of water. Strychnine, ½ gr., hypodermically. Oxygen inhalations. Saline infusion with dextrose for collapse

**Pharmacology.** The action of acetanilide is due to the formation of *p*-aminophenol in the organism, and the drug is excreted in this form in the urine, which is coloured brown. Large doses or continued use result in the formation of methæmoglobin from the hæmoglobin of the blood, leading to cyanosis. Idiosyncrasy sometimes occurs, cyanosis resulting from small doses. Chronic poisoning is indicated by weakness, dyspnoea, sweating, hot flushes, mental depression and rapid heart, sometimes erythematous rashes occur.

Sodium bromide slightly antagonises the antipyretic action of acetanilide. Caffeine raises the temperature of fevered rats and antagonises the antipyretic action of acetanilide. Sodium bromide and caffeine together antagonise to a large extent the antipyretic action of acetanilide—P. K. Smith and W. E. Hambouger, *J. Pharmacol.*, 1935, 55, 205.

**Uses.** Antipyretic and analgesic. Useful in neuralgia, migraine, sciatica and dysmenorrhœa. Applied externally as a dusting powder it relieves the pain of ulcers, but toxic symptoms may occur owing to absorption. Checks the chills and fever of phthisis, and is useful in typhoid. Relieves the darting pains of locomotor ataxy.

[P1] **Pulvis Acetanilidi Compositus (B.P.C.)**

Dose — 3 to 5 grains (0.2 to 0.3 g.)

Acetanilide 7, caffeine 1, sodium bicarbonate 2.

[P1] **Tabellæ Acetanilidi Compositæ (B.P.C.)** Contain acetanilide 2 gr., caffeine  $\frac{1}{2}$  gr., and sodium bicarbonate 1 gr.

[P1 S1] **Tabellæ Acetanilidi Compositæ cum Codeina**

(B.P.C.) As the preceding, with the addition of codeine  $\frac{1}{4}$  gr.

[P1] **Elixir Acetanilidi Compositum.** Dose —  $\frac{1}{2}$  to 1 drachm (2 to 4 ml.)

Acetanilide 326 gr., caffeine 32 gr., tincture of nuxvomica 256 m., aromatic spirit of ammonia 8 oz., aromatic elixir to 16 oz. Filter with aid of talc 120 gr. For headache.

[P1] **Phenalgin** (Etna Chemical Co., London, Pearson, Mitcham) Dose — 5 to 15 grains (0.3 to 1 g.) A mixture with acetanilide as the active base, as an antipyretic and hypnotic. Tablets and gelatin (hard) capsules, 5 grains.

Analysis of Phenalgin gave acetanilide 60%, sodium bicarbonate 25%, ammonium carbonate 15%. Incompatible with calomel and aspirin. Dangerous interaction may occur—J. Noble, *Pharm. J.*, 1922, 151.

[P1] **Methylacetanilidum (B.P.C.)** Prop. Name. EXALGINE (Fr. Ca.).  $C_6H_5N(CH_3)OC_2H_5$  — 149.1

Dose —  $\frac{1}{2}$  to 2 grains (0.03 to 0.12 g.) in solution, cachets or pills. In colourless crystals, with a slight saline taste.

An analgesic, anti-neuralgic, antipyretic (only in unsafe doses). Toxic doses cause paralysis of respiratory organs.

**Soluble** 1 in 60 of water, freely in alcohol, 1 in 10 of ether, 1 in 2 of chloroform.

**Incompatible** with salicylic acid.

**Antidotes.** Treat as for poisoning by acetanilide.

**Anilinum (B.P.C.)** Syn. MONOPHENYLAMINE, ANILINE. Oil  $C_6H_5NH_2$  — 93.1

A colourless (when freshly distilled) oily liquid, with sp. gr. 1.027. Of burning taste, miscible with alcohol and oils, soluble 1 in 37 of water.



**Antidotes.** Empty stomach by stomach tube or emetic  
Fresh air, artificial respiration, oxygen inhalations Strychnine,  
½ gr., hypodermically Saline infusion Venesection followed by  
blood transfusion

Aniline has a direct effect on the heart muscle, producing  
arrhythmia and heart-block Aniline intoxication may be  
produced either by absorption *per os* or through the skin, and in  
its acute stage cardiac and not respiratory treatment is indicated

Poisoning by a boy drinking less than 2 ml of a water and aniline mixture  
Final recovery under oxygen given through a nitrous oxide bag for 5 minutes  
at a time with intervals of 15 minutes, instead of constantly through a funnel  
—far better this way—J. Inkster, *Lancet*, 11/1926, 752

**Paraphenylenediamine.**  $C_6H_4(NH_2)_2=108.1$

[P2] "*Phenylene diamines, toluene diamines, their salts*"

[83] "*Phenylene diamines, toluene diamines, their salts—in substances other than preparations for the dyeing of hair*"

[87] *Preparations for the dyeing of hair containing phenylene diamines or toluene diamines or their salts must be labelled with the words "Caution This preparation may cause serious inflammation of the skin in certain persons and should be used only in accordance with expert advice," instead of the word "Poison"*

Prepared by nitrating acetanilide and subsequent reduction  
with tin and hydrochloric acid In white or reddish crystals  
soluble in water, alcohol and chloroform M p 140°

For use as hair dye, apply first a 2% solution with 1.5% of  
sodium hydroxide, then an oxidising agent, e.g., 5% ferric  
chloride to give brown, or 3%  $H_2O_2$  to produce a black shade

In cases of poisoning by paraphenylenediamine dyes, oedema of head, neck,  
tongue, eyelids and face is the first stage, skin eruptions, eczema, nausea or  
nervous symptoms, sleeplessness, dizziness, weakness, etc., or impairment of  
vision may follow

**Hair Dyes.**—Before applying, the sebum must be removed 1% approx of  
ammonia is said to be safe, but 10% injurious Lead dyes (e.g., lead acetate  
and sodium thiosulphate) are dangerous, as also are silver, e.g., pyro, amidol  
and silver nitrate Pure henna dye is harmless, though penetrating the cortex,  
as also Henna-reng (henna and indigo) As to the paraphenylenediamine  
group, toxic effects are both local and general **Sabouraud-Rousseau's Test**  
is used as a sensitisation test The skin over the mastoid process is cleaned  
with alcohol and then the dye and its oxidant applied When dry cover with  
flexible collodion After 24 hours remove collodion and wash with soap and  
water If patient is sensitive a mild reaction will have formed If dermatitis  
is caused in use as hair dye, or from furs, a simple calamine lotion containing  
2% of ichthammol should be used *Do not attempt to remove the dye by  
hydrogen peroxide or thiosulphate*—R. M. B. Mackenna, *Brit med J*,  
1/1930, 899 Some of these remarks are criticised by A. Mahony-Jones, *ibid*,  
979

Hair dyes and their application—*Lancet*, 1/1929, 1072

Oedema in animals prevented by large repeated doses of strychnine and other  
substances increasing adrenaline output—*J. Pharmacol*, April, 1926, 228

A case of systemic poisoning, with death from sub-acute atrophy of the  
liver, in a girl aged 21, a hairdresser's assistant There was no skin affection  
traceable to the dye Rubber gloves were used when applying the dye, and the  
gloves removed for the subsequent shampoo The staining of the hands was  
removed with hydrogen peroxide, which was possibly a contributory cause, as  
it has been stated that it is most dangerous to remove the dye from the hair  
by the use of hydrogen peroxide or sodium thiosulphate, as these measures  
only intensify the symptoms It seems possible that the production of aniline

is responsible for the toxic symptoms —M C G Israels and W. Susman, *Lancet*, 1/1934, 509

Paraphenylenediamine and other diamines in hair dyes may be detected by tests described by C. Griebel and F. Weiss (*see Analyst*, 1933, 417)

Hair dyes with a base of paraphenylenediamine are so noxious that nearly every European country, as also New York, forbids them —*Lancet*, 11/1927, 824

Inecto Ltd. issue a warning on the use of Inecto, which contains paraphenylenediamine and resorcinol, but this was not sufficient to protect them—later warnings were more complete. Damages £200 —*Brit med J*, 1/1922, 373. A further case. In spite of proved negligence of user, she was awarded £500 plus a further sum as special damages —*Lancet*, 1/1926, 1058

**Dyed Furs.** Fur workers and wearers of dyed fur are liable to be affected with dermatitis from this substance. Investigations show that paraphenylenediamine is almost the only dye used, since it has the advantage of being used cold. The fur is dipped in a 0.5% solution and then into hydrogen peroxide, when "Bandrowski's base" is formed. The fur is then washed in revolving drums. Complete removal of all unoxidised amine should be made compulsory —*Yearb Pharm*, 1924, 524

The result of investigating a large number of cases of fur dermatitis has shown that at least 45% of these cases were due to paraphenylenediamine-dyed furs. Examination of its oxidation products formed during the process of dyeing and of the dyed fur showed that a large amount of Bandrowski base may be formed on the fur, and that the final product of the dyeing is an azine combined with the protein in the fur. Paraphenylenediamine itself, and not any intermediate oxidation products, is stated to be the active irritant in fur dermatitis —H. E. Cox, *Analyst*, 1931, 3

Details of the kind of fur and mode of dyeing of 216 furs suspected of having caused dermatitis. It is suggested that irritation is determined by the abnormal penetration of the diamine through the skin, followed by its local reaction with certain constituents of the blood or serum yet unknown —H. E. Cox, *Analyst*, 1933, 738

Analytical results of the examination of 200 furs alleged to have caused fur dermatitis showed that about half of them contained free paraphenylenediamine in amount from 0.15% downwards, but in 35 cases the furs were undyed, and could not have caused dermatitis. Paraphenylenediamine is a definitely toxic substance, but the product of complete oxidation is harmless —H. E. Cox, *Brit med J*, 11/1933, 255

A normal person may fail to react to a 10% solution of Urol containing p-phenylenediamine, whereas dermatitis cases react to concentrations as low as 0.005%. Who is to be held responsible for this idiosyncrasy? It is difficult to see why a trader who has used proper materials and done his job efficiently should be liable for results so far beyond his control —W. J. O. Donovan, *Brit med J*, 11/1932, 294

[P 83 S7] **Metaphenylenediamine Hydrochloride.** *Syn* METADIAMINOBIENZENE HYDROCHLORIDE, LANTINI  $C_6H_4(NH_2)_2 \cdot HCl$

*Dose* —  $\frac{1}{2}$  grain once or several times daily. In acute diarrhoea the urine becomes dark coloured

It is used for the determination of nitrites in water

This compound is considered more poisonous in furs than the para compound.

**METOL** poisoning due to the presence of the methyl derivative of paraphenylenediamine. Victims of poisoning by phenylenediamines are warned against the use of soap which aggravates the dermatitis. Acetic acid 50% is advocated as a detergent, and for the relief of the itching bathing the parts in cold water is recommended —*Pharm J*, 1/1923, 386

**Benzidine.** White or slightly reddish crystals, m.p. 128. Slightly soluble in alcohol, ether and boiling water. Used as a reagent for detecting certain oxidising agents, especially the oxidase of blood (*see Vol II*)

**Phenylhydrazinæ Hydrochloridum.**

$C_6H_5 \cdot NH \cdot NH_2 \cdot HCl = 144.5$

**Dose.**— $1\frac{1}{2}$  to 5 grains (0.1 to 0.3 g.). 2 gr. per day should rarely be exceeded, and frequently 2 gr. per week is sufficient. Dosage must be controlled by blood counts. Each gramme of phenylhydrazine destroys on an average 6 g of hæmoglobin.

Colourless shining scales, readily soluble in water. *Handle carefully, may produce eczema.*

Phenylhydrazine has a specific effect in destroying erythrocytes and is used therefore in polycythæmia. There is a marked reduction in blood volume directly proportional to destruction of the erythrocytes, and when anæmia has been produced a relative increase in plasma volume is noted.

The action is delayed and may continue for two weeks after administration has been stopped. Administration should cease as soon as the effect is noticed until it is known how far the erythrocyte count will fall.

Has its dangers but is effective. Spleen extract less dangerous, but not known whether equally effective—*Lancet*, 1/1929, 1315.

The erythrocyte count may be kept near normal by 0.1 g. daily to a total of 2.1 g., when the drug may be safely discontinued for 1½ months. In this dosage there is no deleterious effect on the liver—C. L. Stealy, *J. Amer. med. Ass.*, 1/1928, 1289.

In advanced polycythemia vera should not be given, and only with extreme caution to those over 60, patients with marked arteriosclerosis, or advanced visceral injury. Such patients should be given only small doses, 0.1 or 0.2 g. and subsequent dosage determined by symptoms. Less advanced cases do well on 0.1 to 0.3 g. weekly, and the effect observed over several days. Patients who have had thrombosis should be treated cautiously. Ambulatory treatment best, every effort being made to keep circulation as free as possible. Frequent counts of red and white cells and estimations of serum bilirubin needed. As its action continues after withdrawal, it should be stopped before red cell count is normal. Marked rise in bilirubin means excessive blood destruction, and rising leucocyte count indicates great destruction of liver cells. Results transitory and merely palliative—H. Z. Giffin and H. M. Connor, *J. Amer. med. Ass.*, 1/1929, 1507; Hurwitz and Levitus, *ibid.*, 1/1929, 1629.

It is always advisable to omit the drug when the red cell count approaches 6,000,000 per c mm. Should the red cell fall become alarming, blood transfusion will arrest its progress, followed by liver extract. A case described in which four short courses were given without untoward effect, but a fifth produced a severe hæmolytic crisis—A. M. Kennedy, *Brit. med. J.*, 1/1934, 657.

**Acetylphenylhydrazine**,  $C_6H_5 \cdot HN \cdot NH(C_2H_5O)$ . *Syn* PYRODIN, HYDRACETIN, in colourless crystals slightly soluble in water, has also been used.

Equally effective as phenylhydrazine in polycythæmia vera without producing toxic symptoms so readily in similar doses—C. T. Stone, T. H. Harris and M. Bodansky, *J. Amer. med. Ass.*, 11/1933, 495.

**Acidum Sulphanilicum.**  $C_6H_4(NH_2)SO_3H \cdot 2H_2O (1.4) = 209.2$

**Dose.**—10 to 20 grains (0.6 to 1.2 g.)

In small white crystals, slightly soluble in water. Used in Ehrlich's Diazo Test, now superseded by the Widal reaction. Iodism has been treated by 15-grain doses daily in 7 ounces of water, on the erroneous supposition that it reacted with nitrites supposed to liberate iodine from iodides in the body.

It is analgesic, and is best given as—

**Sodii Sulphanilas.**  $C_6H_4(NH_2)SO_3Na, 2H_2O = 231$  1.

*Dose.*—5 to 15 grains (0·3 to 1 g).

In white shining scales, easily soluble in water. Useful in acute catarrh, laryngitis, and otitis. Said to convert the harmful nitrites in saliva and nasal mucus into innocuous diazo bodies.

**Zinci Sulphanilas.** *Prop Name* NIZIN (*Burroughs Wellcome, London*)  
( $C_6H_4NH_2SO_3$ )<sub>2</sub>Zn, 4H<sub>2</sub>O.

White crystals soluble 1 in 6 of water, 1 in 250 of alcohol. Astringent and antiseptic. Solutions 1 in 500 to 1 in 250 are injected in leucorrhœa and gonorrhœa. In atrophic rhinitis the nasal fossæ may be packed with gauze dipped in 1 to 2% solution.

## ACIDUM ACETICUM

$CH_3COOH = 60$  03.

**Acidum Aceticum Glaciale** (*B P, U S P XI*) Contains not less than 99% *w/w* of  $CH_3COOH$  Sp gr 1·055 to 1·058 *P Belg. IV, P Ital V and F E VIII* not less than 96%; *P. Helv. V* 98 to 100%; *P Dan* 96%

A colourless liquid or crystals melting at about 14·7° obtained as a product of the destructive distillation of wood, or synthetically.

**Antidotes.** Stomach tube and emetics must *not* be used. Give a pint of water to which has been added 4 tablespoonfuls of magnesium oxide, or 2 teaspoonfuls of soap dissolved in a pint of warm water (Chalk, sodium bicarbonate or carbonate, well diluted, may be used in absence of magnesium oxide, but it is better to avoid the use of carbonates if possible because the evolution of carbon dioxide may rupture the weakened walls of the stomach.) Milk, white of egg, oil or other demulcents. Morphine,  $\frac{1}{4}$  gr hypodermically, for shock.

**Uses.** Is not given internally. It is applied to corns and warts. Has caustic action, but gives much pain. Psoriasis of a chronic type has been cured in a week or two by glacial acetic acid locally.

**Acidum Aceticum Aromaticum** (*B.P.C.*). *Syn.* AROMATIC VINEGAR. Glacial acetic acid about 74% *v/v*, with odorants. Used as a restorative.

**Acidum Aceticum** (*B P*) 32·5 to 33·5% *w/w*. *U S P XI* is 36 to 37%; *P Helv V* 29·5 to 30·5%, *P. Dan.* 29·5%

*Dose* —5 to 15 minims (0·3 to 1 ml)

*B P* has sp gr. 1·044 to 1·045. *P Austr., P.G. VI* and *P Belg IV* (30%) and *F E VIII* (30%) designate this acid "Dilutum."

**Incompatibles.** Alkalis (hydroxides, carbonates, etc.)

**Use.** Externally for ringworm and in liniments.

**Acetum Odoratum** (*B P C'*) *Syn* TOILET VINEGAR. Acetic acid 1 in 8 with odorants

**Lotio Acidi Acetici** (*R L O H*) Acetic acid 25 m, sterilised water to 1 ounce. Relieves itching and irritation, *e g*, in spring catarrh.

**Vapor Acidi Acetici (T.H.)** Acetic acid and glacial acetic acid, equal parts  
One teaspoonful to a pint of hot water as a sedative inhalation

**Acidum Aceticum Dilutum (B P, U S P XI)** 57 to 63°<sub>w</sub>  
*w/w*

**Dose** — $\frac{1}{2}$  to 1 drachm (2 to 4 ml).

Sp gr about 1.008 (*Fr Cx* is 10%.)

**Uses.** May be given as an antidote to poisoning by alkalis, and, largely diluted, is applied as a lotion for inflamed joints, etc., and to bathe the skin as a refrigerant in cases of fever

**Acetyl Chloride.**  $\text{CH}_3\text{COCl}$  = 78.5 A volatile liquid with intensely penetrating odour, boiling at 51°. Obtained by combining carefully glacial acetic acid 130, with phosphorus pentachloride 137, distilling, and redistilling the fraction passing over below 60°

**Acetamide.**  $\text{CH}_3\text{CONH}_2$  59.05

Deliquescent crystals, m p 82°, made by interaction of ammonia and acetyl chloride

**Æthylis Acetas (B P C, Fr Cx, P Helv V)** *Syn.* ÆTHYL ACETICUS  $\text{CH}_3\text{COOC}_2\text{H}_5$  = 88.06

**Dose** — $\frac{3}{4}$  to 1 drachm (3 to 4 ml) for a single administration,  $\frac{1}{4}$  to  $\frac{1}{2}$  drachm (1 to 2 ml) for repeated administration

Contains not less than 90% *w/w* of ethyl acetate Boiling-range 73.9° to 77.8 Sp gr 0.900 to 0.907

**Soluble** 1 in 15 of water, miscible with alcohol, ether, and chloroform.

Is used as an inhalation in laryngeal catarrh,  $\frac{1}{2}$  drachm to 1 pint of warm water (60°). Internally it is carminative, antispasmodic and diaphoretic Is largely used as a solvent.

**Potassii Acetas (B P, U S P XI)**  $\text{CH}_3\text{COOK}$  = 98.12

**Dose.**—15 to 60 grains (1 to 4 g) *U S P. XI* average dose 15 grains

Deliquescent white crystals, masses or powder Diuretic, and uric acid solvent

**Soluble** 2 in 1 of water, 1 in 2 of alcohol 90%

**Uses.** Is given to render the urine alkaline and as a diuretic Has mild diaphoretic and febrifuge properties.

[P1] **Mistura Potassii Acetatis Composita (B P C)**

*Syn.* MISTURA DIURETICA.

**Dose** — $\frac{1}{2}$  to 1 ounce (15 to 30 ml).

Contains potassium acetate 20 gr, spirit of nitrous ether 30 m, and tincture of hyoscyamus 20 m, with juice of scopolarium in infusion of buchu to 1 oz

**Mist. Diuret. (N I F)**

Potassium acetate 15 gr, potassium nitrate 7 $\frac{1}{2}$  gr, vinegar of squill 20 m, decoction of scopolarium to  $\frac{1}{4}$  oz

**Sodii Acetas (B P C, U S P XI, P Helv V)**

$\text{CH}_3\text{COONa}$ ,  $3\text{H}_2\text{O}$  = 136.07

**Dose** —5 to 20 grains (0.3 to 1.2 g.). *U.S.P. XI* average dose, 25 grains.

Colourless crystals or white powder, efflorescent in warm air Soluble about 1 in 1 of water, with alkaline reaction, and about 1 in 35 of alcohol 90%.

**Uses.** To some extent as a diuretic and as rectal injection in uræmia instead of the bicarbonate. It is excreted as carbonate.

**Acetic Anhydride.**  $(\text{CH}_3\text{CO})_2\text{O} = 102.05$

A colourless liquid with pungent odour, sp gr 1.080 Bp 138°

Obtained by interaction of anhydrous sodium acetate and carbonyl chloride. Is not employed medicinally, but is extensively used in chemical manufacture.

[P1 & 81] **Thallii Acetas (B.P.C.)** Syn THALIOUS ACETATE  
 $\text{CH}_3\text{COOTl} = 263.4$

[P1] and [81] "*Thallium, salts of.*"

**Dose**—0.008 g per kg body-weight ( $\frac{1}{8}$  grain per pound), unless there is marked discrepancy between age and weight, in sweetened aqueous solution.

A white crystalline powder, mp about 131°

**Antidotes.** Empty stomach by emetic or stomach tube. Give purgative dose of magnesium sulphate. Milk in copious draughts. Keep patient warm. Caffeine sodium benzoate, 2 gr hypodermically, for shock. Saline intravenously. Intravenous injection of potassium iodide has been suggested. Sodium thiosulphate intravenously in daily doses, 20 ml of 3% solution slowly (too large doses are to be avoided), promotes gradual elimination of thallium in the urine.

It has been much advocated for **epilation in ringworm**, the direction being to administer it only to children who have not reached the age of puberty in dosage based on weight of the child. Details, see Edn XIX, p. 891. At least 24 deaths are recorded. 3 deaths at Wembley—*Lancet*, 1/1929, 795, 846.

Refs.—*Brit med J*, 1/1928, 659, *ibid*, 1/1930, 589, *Lancet*, 1/1929, 1105. Use not justified—*Lancet*, 11/1930, 1340. A girl bedridden with paralysis from it—*Med Pr*, Dec 10, 1930. Interdicted by Bd of Education—*Brit med J*, 1/1931, 373, 473, 575. Toxic symptoms, 3 cases out of 101—*Lancet*, 11/1931, 913. After-results not encouraging. Anything but epilation by X-ray treatment is a waste of time—L. Haden Guest, *Brit med J*, 1/1932, 261.

20 cases of poisoning with 6 deaths in Mexicans consuming cakes made from barley containing 1% of thallium sulphate (stolen from a government warehouse), used for controlling squirrel infestation. Daily intravenous injections of 5 to 15 grains (or more) of sodium iodide of value for fixation, with sodium thiosulphate intravenously for elimination—J. C. Munch and co-workers, *Amer med Ass*, 1/1933, 1319.

**LOCAL APPLICATION.** Excellent therapeutic effects may be obtained by local application of thallium in children suffering from trichophyton infection of the scalp. Provided the general condition of the child is satisfactory, the hair of the scalp is cut very short and the affected areas rubbed with benzene and ether. The amount of thallium acetate applied varies with the size and extent of the lesions and the weight of the child, but is not more than half the amount which would be given orally in the same patient. The thallium is dissolved in  $\frac{1}{2}$  to 1 ml distilled water to which 4 ml colloid solution is added. The mixture is then placed on the affected areas. After 13 to 15 days the colloid crust is removed. Most of the hair adheres to it and the remainder may be epilated painlessly with forceps. During the following days the scalp is washed daily and 1% iodine solution applied twice daily, followed by Wilkinson's ointment at night. In some cases the fungus disappears within 2½ to 3½ weeks, in others longer. Growth of the hair commences in 4 to 6 weeks, and is complete in 4 months—S. Lieberman, per *Brit J Dermat*, 1936, 45.

[P1 & 81] **Thallium Depilatorium** (*Schering, London*) is a preparation of thallium, available in 1, 10 and 100 mg tablets, for epilation treatment.

**Acetonum** (B.P., U.S.P. XI, P. Jap. IV, F.E. VIII, P. Helv. V) Syn DIMETHYLKETONE  $\text{CH}_3\text{CO}\cdot\text{CH}_3 = 58.05$ .

**Dose**—60 to 90 minims (4 to 6 ml) daily.

A colourless, light, inflammable, neutral liquid, with ethereal odour and camphoraceous taste, obtained by the dry distillation of acetates, also by the destructive distillation of wood and by a fermentation process from maize starch.

It is miscible with water, alcohol, ether, chloroform, and oils, and is a ready solvent of fats and resins, pyroxylin, celluloid and many other organic substances. It takes up about 25 times its volume of acetylene. Sp. gr. is 0.796 to 0.801, b.p.  $56^{\circ}$  to  $58^{\circ}$ . It is largely employed in the manufacture of chloroform. Acetone has been used in dyspnoea. It has also been given as an anthelmintic, and used for cleansing the skin prior to operation.

It occurs in small quantity as a normal constituent in the urine, also (frequently in large amount) in that of diabetics, cf. Vol. II.

**Acetophenonum.**  $C_6H_5 \cdot CO \cdot CH_3 = 120.0$  Syn. HYPNONE, PHENYL-METHYLKETONE.

Dose— $1\frac{1}{2}$  to 5 minims (0.1 to 0.3 ml.) in almond emulsion, or with mucilage or syrup and peppermint water, or in capsules containing  $\frac{1}{2}$  minim.

A colourless liquid, with odour of bitter almonds. Insoluble in water, but soluble in alcohol and oils. Used as an hypnotic it requires care.

**Benzophenonum.**  $(C_6H_5)_2CO = 182.1$  Syn. DIPHENYLKETONE.

Dose.—3 to 8 grains (0.2 to 0.5 g.) White aromatic crystals. Has hypnotic properties.

**Acidum Pyrolignosum Crudum.** A brown acid liquid, the product of destructive distillation of wood. Contains acetic acid 5 to 13% (*P. G. VI* has minimum 8.4%, *P. Helv. V* 6 to 7%) according to the kind of wood used, also other acids—propionic, butyric, etc., also small quantities of methyl alcohol, furfural, pyridine, creosote and resins. Has been employed locally for gangrene and has veterinary uses. It has antiseptic and preservative properties.

**Acidum Pyrolignosum Rectificatum.** Contains about 5% acetic acid. Of yellowish colour becoming darker on keeping. Occasionally ordered diluted 5 to 10% in mouth-washes and gargles.

**Acidum Monochloraceticum.**  $CH_2Cl \cdot COOH = 94.5$

Prepared by chlorination of acetic acid in presence of iodine at water-bath temperature, subsequently fractionating and reserving the  $180^{\circ}$ — $188^{\circ}$  fraction.

Deliquescent white crystals, m.p.  $63^{\circ}$ , or liquefied. It blisters the skin, and is a caustic for warts and corns. **Soluble** with ease in water, alcohol and ether.

In the electrolysis of sodium chloride as used in treatment of gonorrhoea, this acid is less decomposed than the salt, and it is able to neutralise the alkalinity which would deposit against the urethral membrane.

**Acidum Dichloraceticum.**  $CHCl_2 \cdot COOH = 128.9$

A colourless caustic for venereal sores.

**Acidum Trichloraceticum** (*B. P.*, *U. S. P. XI*, *P. Helv. V*, *P. Ned. V*, *P. Jap.*, *P. Dan.*, *F. E. VIII*)  $CCl_3 \cdot COOH = 163.4$ .

Prepared by chlorination of acetic acid, or by the action of fuming nitric acid on chloral hydrate.

In deliquescent crystals, m.p.  $55^{\circ}$  (lower if moist), and boiling at  $195^{\circ}$ , very soluble in water, alcohol and ether.

**Uses.** Applied as a crystal or liquefied by the addition of the minimum amount of water, it is a quick escharotic for venereal

and other warts. As a disinfectant lotion or gargle, 1 to 5% aqueous solution may be used. A solution of 1 part in 2 of glycerin has been employed as a caustic in chronic pharyngitis.

**LARYNGEAL TUBERCULOSIS** treated by trichloroacetic acid—thought specific. The infection is secondary to pulmonary tuberculosis—*Brit med. J. Epit*, 11/1930, 7.

**LEPROTIC LESIONS** treated with applications of a solution—1 in 1 for centre of large thick nodules, 1 in 5 for painting on face, and 1 in 3 generally useful. Must not be too strong or brush too wet. When dry, skin should show a white powdery appearance, otherwise repeat second or third time. May be repeated after 10 days—E Muir, *Indian med Gaz*, May, 1926, 216.

**RIGG'S DISEASE**—incipient stages—This acid applied to the gum after cleaning with hydrogen peroxide solution 10 or 20 volume, is a good remedy. The action is probably dual—killing the infective organisms and dissolving the calcium carbonate of the tartar. With the disappearance of the tartar the presence of bacteria is excluded. Should be tried before sound teeth are sacrificed.

**RODENT ULCER**—A solution of trichloroacetic acid, 3 drachms in 20 minims of water, applied. The acid should be washed off after about 3 minutes, and then for 24 hours no soap or water is allowed on the ulcer. The eschar usually peels off in about 22 days—H Leslie-Roberts, *Brit med. J.*, 1/1927, 794.

**TONSILS, DISEASES OF**—Where operative treatment is not permitted, the use of trichloroacetic acid applied on a right-angled wool-carrier and passed deeply into the crypts, has been found of value in reducing the size of the tonsil and adding to the comfort of the patient.

**Glycine.** *Syn* AMINOACETIC ACID, GLYCOCOLL.

$\text{CH}_3\cdot\text{NH}_2\cdot\text{COOH} = 75.05$ .

**Dose.**—150 grains to 1 ounce (10 to 30 g) per day, in two or three doses.

White crystals with sweet taste, **soluble** in water 1 in  $4\frac{1}{2}$ , slightly in alcohol, insoluble in ether. M. p.  $234^\circ$ . It is both acidic, by reason of its acid group, and basic by reason of its amino grouping. It forms double salts with soluble metallic chlorides and nitrates.

The name "glycin," though applied in chemistry to this body, was given to *p*-oxyphenylaminoacetic acid,  $\text{C}_6\text{H}_4\cdot\text{OH}\cdot\text{NHCH}_2\cdot\text{COOH}$ , used in photography as a developer. Confusion may be avoided by the use of the name "glycocoll."

**Uses.** Of value in the treatment of myasthenia gravis. The muscular weakness is connected with a failure to convert creatine into creatinine, for which the presence of an amino-acid is necessary. Glycine produces an increase in the output of creatinine and a drop in the excretion of creatine. Is effective in some cases of myasthenia gravis in which ephedrine fails. Other cases are benefited by the supplementary administration of ephedrine,  $\frac{1}{8}$  to  $\frac{1}{2}$  gr., given 20 minutes later (the total daily amount should never exceed  $1\frac{1}{2}$  gr.).

Glycine may be prescribed in an inexpensive form as gelatin. Thus 80 g of gelatin boiled to a pulp may be ordered daily. The glycine content is approximately 25%.—D. McAlpine, *Lancet*, 1/1934, 180.

**Choline.**  $\text{HO}\cdot\text{N}(\text{CH}_3)_3\cdot\text{C}_2\text{H}_5\cdot\text{OH} = 121.1$ .

A non-poisonous syrupy fluid. A decomposition product of lecithin. It stimulates intestinal movements.



Choline is essential for liver function, lack of it causes fatty degeneration. Dogs with the pancreas removed died in a few months when treated with insulin alone, but survived for years when fed with minced pancreas (which contains choline) in addition. Diabetes is a disorder of the liver rather than of the pancreas, and may be caused by an over-active liver due to disease or to deficiency of insulin, or to over-active pituitary, thyroid or adrenal glands—C. H. Best, *Science (Suppl.)*, 1/1935, 2112

**Choline Chloride.** *Syn* CHOLINE HYDROCHLORIDE

$\text{Cl N}(\text{CH}_3)_3 \text{C}_2\text{H}_4 \text{OH} = 139.6$

*Dose.*—10 grains (0.6 g) intravenously

Deliquescent needles soluble in water and alcohol

**ILEUS** treated by choline hydrochloride. It acts on the hormone of intestinal movement. That it is specific in its action on the intestine is shown by the fact that it does not affect the rhythm of the heart or of the uterus. In practice it is well to make ampoules containing 0.6 g of the hydrochloride in 6 ml. This solution is diluted with 180 ml of normal saline, and given intravenously. At least 17 minutes should be employed to administer the whole of the solution. The treatment re-established normal function in some cases—C. G. L. Wolt and J. R. C. Canney, *Lancet*, 1/1926, 707

**Bakolyse** (*Anglo-French Drug Co., London*). A sterile solution of amino-acids and creatinine for intramuscular or subcutaneous use in tuberculosis and all states of denutrition. *Dose*—2 ml every 3 or 4 days with a minimum of 20 injections

**Biocholine** (*Robert & Carrière, Paris, Anglo-French Drug Co., London*). Solution of choline hydrochloride for injection. *Dose*—1 ml (= 0.01 g) subcutaneously every two days continuously. In the treatment of all forms of tuberculosis

[P181] **Ergocholin** (*Wiernik, Berlin, Coates & Cooper, London*). Tablets containing 0.008 g of Pacyl and 0.0005 g of ergot alkaloids. *Dose*—One tablet three times daily. In thyrotoxic conditions

**Lyocholin** (*Richter, London*). Choline hydrochloride 0.02 g. *Dose*—1 ml injected daily. Tuberculosis, hypertension

**Pacyl Tablets** (*Wiernik, Berlin, Coates & Cooper, London*). *Dose*—1 or 2 tablets twice or three daily, commencing with the smaller dosage—to be swallowed whole and followed with water

A choline preparation, each tablet containing  $\frac{1}{2}$  grain (0.005 g), employed to reduce blood pressure in arteriosclerosis, chronic nephritis and the climacteric

**Sedicyl Tablets** (*Wiernik, Berlin, Coates & Cooper, London*). *Dose*—1 or 2 tablets three times daily—subsequently 2 tablets a day. A choline derivative used at the climacteric

**Sterules Choline Chloride** (*Martindale, London*). Ampoules containing a solution of 0.6 g in 6 ml, for dilution with normal saline

**Acetylcholine.**  $(\text{CH}_3)_3\text{N}(\text{OH})\text{C}_2\text{H}_4\text{COOCH}_3 = 163.1$  The acetyl derivative of choline.

Usually employed as **acetylcholine chloride** or **hydrochloride**,  $(\text{CH}_3)_3\text{N Cl C}_2\text{H}_4\text{COOCH}_3 = 181.6$ . A white hygroscopic powder forming a stable solution in water

*Dose.*— $\frac{1}{2}$  grain (0.05 g) subcutaneously or intramuscularly, and  $1\frac{1}{2}$  grains (0.1 g) the following day. If inadequate after 10 days, increase to 0.2 g twice daily. Average course 15 days' treatment per month for 2 or 3 months. *Dangerous intravenously and ineffective orally*

**Uses.** Has powerful vasodilator effect, which is confined to the arteries and arterioles, and is of value in intermittent claudication, Raynaud's syndrome, gangrene arising from arteritis, and in the complications of arterial hypertension. Tuberculous

sweats yield to doses of 0.01 to 0.02 g, larger doses must be avoided

*Twenty years after physiological activity was known the drug came into clinical use* It produces dramatic relief in various forms of arterial spasm. Of benefit in early arthritis deformans, hemiplegia, trophic ulcers, hyperidrosis, lead colic, etc. Unstable in aqueous solution. Has no cumulative action, and may be given for months without ill effects. A valuable and interesting remedy for which other clinical uses will probably be discovered in time.—Editorial, *Brit med J*, 11/1930, 1011

**EMBOLISM**—Subconjunctival injections of acetylcholine solution the best form of treatment for embolism of the retinal artery—4 minims on the lower temporal quadrant and 4 minims in the lower nasal quadrant, as far back as the equator of the globe—H. C. Orr and J. H. Young, *Brit med J*, 1/1935, 1119

**EPILEPSY**—Daily subcutaneous injections of acetylcholine bromide of 0.1 g for 7 days and 0.3 g for 7 days plus 2 Pacyl tablets daily, failed to substantiate improvement in reduction of epileptic fits recorded in French journals.—F. L. McLaughlin, *Brit med J*, 1/1933, 998. Does not diminish the number of epileptic fits.—J. E. S. Lloyd, *Brit med J*, 1/1933, 999

**HEADACHE** following lumbar puncture can be readily relieved by hypodermic injection of 0.02 g of acetylcholine. The dose may be repeated if necessary.—Lemaire and Bioy, per *Prescriber*, 1936, 89

**HYPERPIESIS** without marked arterial change treated. Semi-permanent fall in blood pressure produced—A. H. Douthwaite, *Brit med J*, 1/1930, 742

**PARALYTIC ILEUS**—Most patients with severe post-operative distension, gas pains, and paresis of the bowels are considerably improved by administration of acetylcholine intramuscularly. In paralytic ileus it appears to be almost specific in curing the condition.—A. L. Abel, *Lancet*, 11/1933, 1252. Value confirmed by K. Heritage, *ibid*, 1258

**Acécoline** (Lematte, Paris, Anglo-French Drug Co, London). A stable solution of acetylcholine in 1 ml ampoules containing 0.02, 0.05, 0.1 and 0.2 g. Average dose—0.1 g twice daily, for 15 injections

**Acécolex** (Lematte, Paris, Anglo-French Drug Co, London). An ointment containing 2% of Acécoline with the addition of fenchone as an antiseptic for the treatment of varicose ulcers, atonic wounds and dermatosis

**Tonocholin** (Richter, London). Acetylcholine hydrochloride. Dose—1 ml (0.05 g) subcutaneously or intravenously on alternate days

**Pragmoline** (Pharmaceutical Specialties (May & Baker) Ltd, London). Acetylcholine bromide. Supplied in solutions of two strengths, "A" 6%, "B" 12.5%. Given by deep subcutaneous injection, or intramuscularly, in hypertension, Raynaud's disease and tuberculous sweats

[P1] **Hypotan** (Lematte, Paris, Anglo-French Drug Co, London). Methyl-acetylcholine bromide 0.005 g, bromocholine bromide 0.005 g, chloral hydrate 0.05 g. Dose—4 to 6 tablets daily before meals for 15 days each month. In hypertension

**Doryl** (Merck, Darmstadt, Martindale, London). Carbaminoylcholine chloride—the urethane of choline. Dose—0.001 to 0.004 g per os, 0.00025 g hypodermically. Uses as for acetylcholine, but fully active orally in above doses and with more persistent action. Also advocated as eye-drops for decreasing intraocular pressure in glaucoma and as a 0.05% solution for local application in ozena

**Acetyl-β-methylcholine chloride**, a synthesised choline derivative, should be employed preferably in all cases when acetylcholine could be used. Subcutaneously produces a prompt and vigorous fall in blood pressure, rise in pulse rate, flushing, sweating and salivation. The action begins within a minute or two of injection, lasts 2 or 3 minutes, and has ceased in 15 to 20 minutes. Caused immediate termination of 25 attacks of paroxysmal tachycardia in 9 patients, the dose varying between 0.005 and 0.05 g. Any untoward effects quickly abolished by injecting atropine.—I. Starr, *Amer J med Sci*, Sept, 1933, 330

A warning as to confusion with acetylcholine. Given subcutaneously, acetyl-β-methylcholine is somewhere between 10 and 20 times as powerful as acetylcholine, and an injection of 75 mg to a boy of 14 would probably

produce enough vagus effect to stop the heart altogether. In cases of overdosage, atropine should be ready at hand.—I Starr, per A B Stenhouse *Lancet*, 1/1936, 391

#### Cysteine.

An amino-acid prepared from the hair of man. Used in the treatment of cutaneous ulcers, employing a 15% solution, containing equal parts of normal saline solution and distilled water, for each gramme of cysteine 6.35 ml of normal sodium hydroxide is added, giving a neutral solution. It is used when fresh, dressings being changed twice daily or more often if required.—L A Brunsting and D G Simonsen, *J Amer med Ass*, 11/1933, 1937

### ACIDUM ACETYL SALICYLICUM

B P, U S P XI, *Fr. Cx.*, P G. VI, *P. Helv* V, *P. Dan.*, *P Ital* V, *P. Svec.* X, *FE* VIII, *P Belg* IV.



**Syn.** ASPIRIN. This name is public property in Great Britain and Northern Ireland. In other countries it is a registered trade mark. ASPIRINOIDS (*Bayer Products, London*) is, however, still on the British Register. ASPRO (*Gollin, Slough*), EMPIRIN (*Burroughs Wellcome, London*), GENASPRIN (*Genatosan, Loughborough*), are further names for the substance in tablet form. ASPIRGRAN (*Monsanto Chemicals Ltd, London*) is a granular form suitable for compression into tablets.

**Dose.**—5 to 15 grains (0.3 to 1 g.), in cachets, tablets, or suspended in a good draught of water thrice daily after meals—not on an empty stomach. Children  $\frac{1}{2}$  to 5 grains (0.03 to 0.3 g.) *P Ital.* V has 3 g. as max. dose in 24 hours, *F.E.* VIII, 5 g.

**Manufacture.** By action of acetic anhydride on salicylic acid. Salicylic acid 50 and acetic anhydride 75 are heated to 150° for two hours under a reflux condenser. On cooling, the crystals are pressed out and recrystallised from dry chloroform. Alternatively, salicylic acid 25 and acetyl chloride 20 are heated under a reflux condenser to 80° for some hours. Excess of acetyl chloride is removed on the water-bath and the product recrystallised from dry chloroform, benzene or carbon tetrachloride.

A white powder, m.p. 135° to 138°. It is not an absolutely stable body—all samples have more or less odour of acetic acid.

**Soluble** about 1 in 300 of water, 1 in 5 of alcohol 90%, 1 in 17 of chloroform, 1 in 20 of ether.

**Incompatible** with free acids, iron salts and alkalis. It forms a clear mixture with sodium bicarbonate, owing to formation of sodium acetate and salicylate, and is not intended to be thus prescribed. Heating the acid in presence of moisture also causes dissociation. For potassium citrate in conjunction *v. postea*.

**Antidotes.** Empty stomach by emetic, or by stomach tube using 5% sodium bicarbonate solution. Keep patient warm. Give milk or water freely, containing a little sodium bicarbonate. Stimulants if necessary. Saline infusion, with dextrose, if required.

**References to Poisoning.**

The dangerous dose of aspirin probably varies considerably around 400 to 500 gr., but, in the light of more recent observation on the beneficial results of treatment, lethal effect may be avoided, even when more than 500 gr. are ingested.

It seems reasonable to believe that even when the symptoms of poisoning have reached an advanced stage, the combined therapeutic effect of the introduction of fluid to the body and the simultaneous aspiration of cerebrospinal fluid will be the means of saving an otherwise hopeless situation.

Notes on four fatal cases and on two cases with recovery following the taking of 500 and 435 gr. respectively — A. V. Neale, *Brit. med. J.*, 1/1936, 110.

Case of woman who took about 435 gr. of acetylsalicylic acid ending in recovery, glucose, 5% in saline, by rectum and fruit juice with glucose by mouth, were given freely. Strikingly beneficial effect of lumbar puncture — S. C. Dyke, *Lancet*, 11/1935, 613.

Attempted suicide by taking 600 gr. Recovery without active treatment — S. Lipetz, *Brit. med. J.*, 1/1934, 652.

Attempted suicide from 450 gr. Cyanosis, and later œdema and enlargement of heart. Recovery — *Lancet*, 1/1933, 490.

**Toxic Effects.** May occasionally cause gastric pain, vomiting and giddiness, œdema of face and skin rash, even in relatively small doses. It should be administered on a full stomach.

**Uses.** Analgesic, antipyretic, and has anti-rheumatic properties. Does not irritate the mucous membrane of the stomach, and is to be preferred to salicylates in heart and ear complaints. Is useful in influenza (especially with quinine), acute and chronic affections of the joints, headaches, and in gout, neuralgia, chorea, and pleurisy. Has been used in hay fever, diabetes and dysmenorrhœa. The gradual hydrolysis of the substance in the body is said to prevent the cumulative toxic action of the salicylic acid. It relieves the pain of cancer and of cystitis.

In influenzal complaints a dose taken at bed-time will often induce perspiration, quiet sleep follows, fever is reduced and pulse improves. In some cases, it is useful with caffeine or with phenacetin and Dover's powder. The latter combination is useful also in measles and mumps, and cuts short incipient lobar pneumonia.

Aspirin gargle (10 gr. to 1 oz. of water) is very useful after tonsillectomy and operations on the pharynx.

**ACUTE RHEUMATISM.** Aspirin in the same dosage would appear to be equally efficacious, if not more so, than sodium salicylate, in reducing pain and fever, but less frequently produces signs of poisoning, and there would appear to be no need to give alkalis with this drug. Yet it must be remembered that some pharmacologists consider aspirin to be more toxic than sodium salicylate. Clinical experience, however, hardly supports this view, and we have come to regard aspirin as the more useful of the two drugs — C. Bruce Perry, *Med. Pr.*, 1936, 136.

**Mistura Acidi Acetylsalicylici (B.P.C.)** *Syn* ASPIRIN MIXTURE.

*Dose.*— $\frac{1}{2}$  to 1 ounce (15 to 30 ml.).

Acetylsalicylic acid 15 gr. suspended with compound powder of tragacanth in chloroform water to 1 oz.

**Mistura Acidi Acetylsalicylici Composita (B.P.C.)** *Syn* COMPOUND ASPIRIN MIXTURE.

*Dose.*— $\frac{1}{2}$  to 1 ounce (15 to 30 ml.).

Acetylsalicylic acid 15 gr dissolved with the aid of potassium citrate 30 gr in syrup of lemon and chloroform water to 1 oz

**Mist. Acid. Acetylsal. (N I F)**

Acetylsalicylic acid  $7\frac{1}{2}$  gr, potassium citrate 15 gr, chloroform water to  $\frac{1}{2}$  oz

**Hustus Acidi Acetylsalicylici Compositus (Mid H)**

Acetylsalicylic acid 5 gr, phenacetin 5 gr, caffeine citrate  $2\frac{1}{2}$  gr, compound powder of tragacanth 10 gr, chloroform water to 1 oz

**[P1] Mistura Acidi Acetylsalicylici Composita (W H)**

*Syn* MORGAN'S MIXTURE

Acetylsalicylic acid 5 gr, caffeine citrate 2 gr, potassium citrate 20 gr, camphorated tincture of opium 15 m, liquid extract of liquorice 15 m, chloroform water to  $\frac{1}{2}$  oz

Aspirin mixtures should not be kept more than a few days actually, the aspirin is hydrolysed in proportion to time (see Vol II)

**Potassium Citrate with Aspirin.** Aspirin in presence of potassium citrate has its solubility in water markedly increased. To make aspirin soluble approx 1 in 20 it is necessary to prescribe nearly twice the amount of potassium citrate with it. In influenza the alkaline effect of potassium citrate is beneficial.

Apart from the action of the potassium citrate the aspirin may be absorbed more rapidly from the stomach and this may give enhanced effect

**Tabellæ Acidi Acetylsalicylici (B P C)** contain 5 gr (0.3 g)

**Tabellæ Acidi Acetylsalicylici et Caffeinæ (B P C)** contain acetylsalicylic acid 4 gr and caffeine 1 gr

**Tabellæ Acidi Acetylsalicylici Compositæ (B P C)** *Syn* COMPOUND ASPIRIN TABLETS. Contain acetylsalicylic acid  $3\frac{1}{2}$  gr, phenacetin  $2\frac{1}{2}$  gr and caffeine  $\frac{1}{2}$  gr. To be distinguished from Tab. Acid. Acetylsal. Co (N I F) which contain Dover's powder (*vide infra*)

**Tab. Aspirin et Phenacetin (N I F)**

Acetylsalicylic acid  $2\frac{1}{2}$  gr, phenacetin  $2\frac{1}{2}$  gr, caffeine 1 gr

**[P1 81] Tabellæ Acidi Acetylsalicylici et Opii (B P C)** *Syn* TABLETS OF ASPIRIN AND DOVER'S POWDER

Contain acetylsalicylic acid  $2\frac{1}{2}$  gr and powder of ipecacuanha and opium  $2\frac{1}{2}$  gr (*Exempt* [D].)

**[P1] Tabellæ Acidi Acetylsalicylici et Opii Compositæ (B P C)** contain acetylsalicylic acid 3 gr, phenacetin  $1\frac{1}{2}$  gr, and powder of ipecacuanha and opium 1 gr

**[P1 81] Tab. Acid. Acetylsal. Co. (N I F)**

Acetylsalicylic acid 6 gr, powder of ipecacuanha and opium 2 gr, phenacetin  $2\frac{1}{2}$  gr (*Exempt* [D].)

**[P1 81] Pilula Aspirin et Acidi Arseniosi (Hoedemaker's Pill) (Vic Park)**

Aspirin  $2\frac{1}{2}$  gr, arsenic trioxide  $\frac{1}{2}$  gr, starch and distilled water sufficient to make into 100 pills. *Dose*—2 pills thrice daily, increasing carefully by one pill every second day to a maximum, continued for a period, of never more than 25 pills daily, and then reducing at the same rate.

**Proprietary Combinations of Acetylsalicylic Acid**

**Anadin (Anadin, London)** Tablets, containing in each aspirin 3 gr, phenacetin 3 gr, caffeine  $\frac{1}{2}$  gr, quinine sulphate  $\frac{1}{2}$  gr

**Ariphon (Lilly, London)** Aspirin  $2\frac{1}{2}$  gr, sodium citrate 5 gr, caffeine citrate  $\frac{1}{2}$  gr, in capsules

**Bromalgin (Reynolds & Branson, Leeds)** Contains aspirin, caffeine citrate and potassium bromide. *Dose*—1 or 2 drachms, well diluted. A general analgesic.

**Collopyrin (British Colloids, London)** Acetylsalicylic acid 5 gr with kaolin. *Dose*—1 or 2 tablets three or four times daily

**Calcii Acetylsalicylas (B.P.C.)**

$(\text{CH}_3\text{CO OC}_6\text{H}_4 \text{COO})_2\text{Ca}, 2\text{H}_2\text{O} = 434.2$  *Prop Names* KALMOPYRIN (*Richter, London*), TYLCALSIN (*Martindale, London*)

*Dose* —5 to 15 grains (0.3 to 1 g.)

White amorphous non-hygroscopic powder, decomposing in moist air

**Soluble** 1 in 6 of water, but it dissociates in proportion to time and temperature in this form, 1 in 800 of alcohol 90%. It is preferably given in *tablet, crushed at the time of taking, in water, or as a cachet, followed by a draught of water*

**Uses.** In view of its greater solubility, calcium acetylsalicylate forms a useful alternative to aspirin. It is more readily absorbed, is often better tolerated and causes less renal irritation.

A prompt rheumatic and influenza specific, also in catarrhs and neuralgia and for relief of pain. Antipyretic action occurs in about an hour, with drop of temperature of  $0.4^\circ$  to  $0.8^\circ$ , the fall being maintained for 2 to  $2\frac{1}{2}$  hours, then give further dose. As analgesic one tablet suffices, two may be given if heart action is normal.

In lumbago 2 tablets at night in hot tea (as diaphoretic) valuable. In gonorrhœal rheumatism has given excellent results.

ASTHMA well treated by calcium acetylsalicylate 10 gr three or four times a day. Calcium lactate used for children —A. M. Bremner, *Brit med J*, 11/1922, 666.

CHORRA. Satisfactory clinical results with an average daily dose *per os* of from 30 to 45 gr of calcium aspirin for a child of 12. It has a triple action: (1) antirheumatic, (2) correction of Ca deficiency, (3) sedative to brain —N. Mutch, *Brit med J*, 11/1944, 248. See also N. Hill, *Med Pr*, 1936, 415.

NEURITIS AND NEURALGIA. Calcium acetylsalicylate 5 gr, quinine salicylate 1 gr, salol 5 gr, and Phenalgin 10 gr, as a combined powder, has been found most efficient.

**Calcium Acetylsalicylate Intravenously.**

*Dose* —The usual dose is 0.5 g in 10 to 20 ml of sterile water, but larger doses, even 2 g, have been injected **very slowly**. Solutions must not be heated. The concentration is of importance, it should not exceed 5%.

**Uses.** Successful in sciatica, acute rheumatism, tabes dorsalis, interstitial keratitis, acute iritis, gonorrhœal synovitis, dysmenorrhœa and severe headaches of doubtful causation. Psoriasis of 15 years' standing was treated by the method with marvellous result, the affection cleared up completely. In obstinate influenza the procedure is worthy of trial. Of considerable value in rheumatic endocarditis. 0.25 g has been given to children of 14.

In acute and subacute rheumatism and in septicæmia useful intravenously —H. Pritchard, *Brit med J*, 1/1927, 794.

Rapid results in rheumatic infections from Tylcalsin intravenously —J. Burnford, *Lancet*, 1/1931, 351. (Not calcium salicylate, as stated.)

**Alasil Tablets** (*Wander, London*) *Dose* 1 or 2 thrice daily in an ample supply of water.

Tablets containing calcium acetylsalicylate  $7\frac{1}{2}$  gr and Alocol (colloidal aluminium hydroxide) 6 gr. Antipyretic, analgesic and sedative. In rheumatic affections, influenza, chills, neuralgia and cough.

If free perspiration is desired 2 tablets should be stirred into a wineglassful of water and taken as a draught at bed-time, followed at once by a tumblerful of hot lemon-water, hot milk, or other hot beverage

Gives immediate relief in gastric influenza—stops the vomiting, relieves the headache, and brings down the temperature—G. H. Wood, *Practitioner*, 11/1933, 112

**Calcium Aspirin** (Genasprin Brand) *Syn* CALCIUM ASPIRIN (Coplans) (*Genatosan, Loughborough*) A brand of calcium acetylsalicylate stabilised by the addition of calcium chloride 15%

**Kafalgol** (*Richter, London*) Calcium acetylsalicylate 0.5 g, caffeine 0.05 g  
Dose—2 to 3 tablets daily In headache, toothache, etc

### **Lithii Acetylsalicylas (B P C).**

$\text{CH}_3\text{CO}\cdot\text{OC}_6\text{H}_4\cdot\text{COOLi} = 186.0$ . *Prop. Names.* HYDROPYRIN (*Richter, London*), LITMOPYRIN (*A Bishop Ltd, London*), TYLLITHIN (*Martindale, London*)

Dose.—5 to 15 grains (0.3 to 1 g). Maximum daily dose 75 grains

White powder with bitter taste

**Soluble** 1 in 1 of water, 1 in 4 of alcohol 90%, insoluble in ether. The salt is to be kept in a well-closed bottle as it undergoes decomposition in moist air

**Incompatible** with iron salts, mineral acids and alkalis  
It is preferably given as cachets or tablets, the latter to be crushed and taken in a little water It is *not desirable* to give it in mixture form

**Uses.** Analogous to those of the calcium salt

**Enema Sédativum** (*St G H*)

Sodium bromide 1 dr, lithium acetylsalicylate 10 gr, water to 5 oz To be mixed with an equal quantity of warm water and given immediately after operation

### **Magnesii Acetylsalicylas.**

$(\text{CH}_3\text{CO}\cdot\text{O}\cdot\text{C}_6\text{H}_4\cdot\text{COO})_2\text{Mg} = 382.3$  *Prop Names* MAGISAL (*Martindale, London*), NEOHYDROPYRIN (*Richter, London*)

Dose—5 to 15 grains (0.3 to 1 g)

Microcrystalline powder, non-hygroscopic, almost tasteless and odourless, soluble 1 in 12 of water, less readily in alcohol

**Incompatibility** and **Uses** are similar to those of the lithium and calcium salts

**Magsyn** (*Allen & Hanburys, London*) Tablets containing  $7\frac{1}{2}$  gr of basic magnesium acetylsalicylate Dose—1 to 3 tablets

**Sodii Acetylsalicylas.**  $\text{CH}_3\text{CO}\cdot\text{O}\cdot\text{C}_6\text{H}_4\cdot\text{COO Na} = 202.1$

*Prop. Name.* TYLNATRIN (*Martindale, London*)

Dose.—5 to 15 grains (0.3 to 1 g.)

White amorphous hygroscopic powder, very soluble in water

**Used** for the same purposes as the calcium salt

**Saligenin.**  $\text{C}_6\text{H}_4\text{CH}_2\text{OH OH} = 124.1$ . Dose—10 grains (0.6 g)

This is the alcohol of which salicylic acid is the corresponding acid It is converted into the acid in the body

It is formed with glucose on the hydrolysis of salicin In acute rheumatism it has been well spoken of by R Stockman

### **Acetylmethyl Salicylas.**

*Syn.* SALACETOL, ACETOLUM SALICYLICUM (*P. Helv V*)

$\text{C}_6\text{H}_4(\text{OH})\cdot\text{COO}\cdot\text{CH}_2\text{CO}\cdot\text{CH}_3 = 194.1$ .

Dose.—10 to 30 grains (0.6 to 2 g.) in cachets or suspended.

In shining crystals very slightly soluble in water, in alcohol 90% 1 in 14 easily. Caustic alkalis decompose it, forming salicylates. Used in rheumatism. For diarrhoea best given in castor oil (if required) before breakfast.

**Alexipon** (*Richter, London*) Ethyl acetylsalicylate. For local application in rheumatism and lumbago.

**Aspriodine** (*Martindale, London*).

Acetyliodosalicylic acid, a stable iodine derivative of acetylsalicylic acid containing about 41% of I. For rheumatic affections and arteriosclerosis. Dose—5 grains (0.3 g.) per day after food, preferably given alone; may be increased if required. Cachets, capsules and tablets are available.

**Methyl-Aspriodine** is methyl acetyliodosalicylate, the methyl ester of Aspriodine. It occurs as white crystals agglomerated into granules, m.p. 40°, containing 39.7% of I. Applied by inunction, it is a prompt local analgesic in rheumatism, neuritis, sciatica, lumbago and other painful affections. Should not be rubbed vigorously into extensive areas unless diluted.

**Methyl-Aspriodine Balm** contains 50% of Methyl-Aspriodine in a lanolin base.

**Methyl-Aspriodine Injection** is a 10% solution in olive oil. Dose—1 ml.

**Methyl-Aspriodine Liniment** contains 25% of Methyl-Aspriodine with camphor, chloroform and menthol.

**Methyl-Aspriodine Pigment** is a 2% solution of Methyl-Aspriodine in a glycerin-alcoholic solvent. Is suitable for inflamed gums.

**Phenyl-Aspriodine** is acetyliodosalol, for use as an intestinal and urinary antiseptic.

Dose.—5 grains (0.3 g.), administered alone as a cachet, capsule or tablet, in water.

**Sedasprin** (*Martindale, London*).

Acetylbromosalicylic acid, a stable compound containing approximately 31% of Br. It combines the analgesic and antipyretic properties of aspirin with the sedative action of the bromides. For use in headache, dysmenorrhœa, insomnia, tonsillitis, etc. Dose.—5 to 10 grains (0.3 to 0.6 g.), preferably given alone as a cachet, capsule or tablet.

**Phenyl-Sedasprin** is acetylbromosalol, the bromine analogue of Phenyl-Aspriodine, containing approximately 24% of Br. A urinary antiseptic, useful also in rheumatic affections, neuralgia, tonsillitis, etc.

Dose.—5 grains (0.3 g.), preferably given alone in a cachet, capsule or tablet, with water.

**Ammonium Ortho-iodoxybenzoate.**

$C_6H_4(IO_2) \cdot COONH_4 = 297.0$ . *Syn* AMIODOXYL BENZOATE.

A white crystalline powder containing 42.7% of I, readily soluble in water. To avoid decomposition it should be kept dry and away from sunlight. Dose.—11 to 15 grains (0.75 to 1 g.) intravenously, or twice this dose orally.

**Uses.** Chiefly in arthritis especially active infection. It is



given in 100 ml. of normal saline intravenously within 7 to 12 minutes, but orally and in 2 g. doses by high enema it has been found effective. Following intravenous use, reactions resembling non-specific protein reactions may occur. The salt is quickly reduced in the blood stream, and it is stated to stimulate phagocytosis of streptococci and staphylococci.

**Arthrytin** (*Pharmaceutical Specialties (May & Baker) Ltd., London*) Calcium *o*-iodoxybenzoate. Tablets contain 0.5 g. Dose—1 tablet with a glassful of water thrice daily after meals. Treatment should be continued for a number of months. For the hypertrophic and atrophic types of arthritis. Good results have also been obtained in leg ulcer. The ammonium salt is also available for intravenous use. Oral administration of the calcium salt is stated not to be followed by the reactions associated with intravenous administration of the ammonium salt.

**Calsiod** (*Menley & James, London*) Calcium *o*-iodoxybenzoate. Tablets contain 0.5 g. Arthritis and rheumatic conditions.

### Acetyl-para-amidosalol.

$C_6H_4OH \cdot COO \cdot C_6H_4NH \cdot COCH_3 = 271.1$  Prop Name SALOPHEN (*Bayer Products, London*) (P Belg, P Helv V, P Ned V, FE VIII, P Ital V, P Svec)

Dose—5 to 15 grains (0.3 to 1 g.) 3 or 4 times a day in cachets.

White crystalline scales, tasteless, soluble in alcohol, ether, and alkalis, almost insoluble in water. It contains about 50% salicylic acid.

**Incompatible** with alkalis and their carbonates. It is unaffected by gastric juice, but decomposed by pancreatic ferment. Febrifuge and antirheumatic. Used in chorea, neuralgia, sciatica, headache and throat affections. Ointment 10% in lanolin for psoriasis and other skin affections.

## ACIDUM BENZOICUM

B P, U S P XI, P Helv V, P Dan, etc

$C_6H_5 \cdot COOH = 122.05$

Dose—5 to 15 grains (0.3 to 1 g.)

**Manufactured** either from gum benzoin (natural) or from toluene (synthetic), the former being the more expensive.

**Soluble** 1 in 450 of water, 1 in 3 of alcohol 90%, 1 in 7 of chloroform and 1 in 30 of glycerin, very soluble in fats and oils.

**Incompatible** with ferric salts and mercuric chloride.

**Uses.** Benzoic acid is an antiseptic, a stimulating expectorant, antipyretic and diuretic. It is given in cases of chronic cystitis, urinary calculi and incontinence, also for rheumatism. It acidifies the urine but is mostly employed in form of one of its salts—*v. postea*. It prevents fats becoming rancid, as in *Adeps Benzoïnatus, q v.*

Four grains of benzoic acid with 1 grain of Canada balsam, or 1 minim of glycerin, makes a good pill.

A 1 in 20 solution in alcohol relieves urticaria, and, as an antiseptic lotion or gargle, 1 dissolved in 500 of water is employed.

**Collutorium Acidi Benzoici (R D H)**

*Dose* —One tablespoonful in a tumblerful of water

Benzoic acid 10 gr, tincture of krameria 15 m, saccharin 6 gr, oil of pepper-mint 2 m, oil of cinnamon 2 m, alcohol 90% to 1 oz

**Miller's Mouth Wash** is similar

**Trochisci Acidi Benzoici (B P C)**

Contain  $\frac{1}{2}$  grain with fruit basis, are also obtainable with simple basis. Those of *T H* have a red currant basis. Useful as a voice lozenge

**Unguentum Acidi Benzoici Compositum (B P C)** *Syn* WHITFIELD'S OINTMENT

Contains benzoic acid 5% and salicylic acid 3% in white soft paraffin and coconut oil

**Unguentum Acidi Benzoici et Acidi Salicylici Forte (K C H)**, also with *Syn* WHITFIELD'S OINTMENT, contains benzoic acid 1 dr, salicylic acid 30 gr, soft paraffin 2 dr, coconut oil to 1 oz

**Ammonii Benzoas (B P C, U S P XI, P Helv V)**

$C_6H_5COONH_4=139.08$

*Dose* —5 to 15 grains (0.3 to 1 g)

In colourless laminar crystals **soluble** 1 in 6 of cold water, 1 in 30 of alcohol, and 1 in 8 of glycerin

Useful expectorant in chronic bronchitis, also used for increasing the acidity of the urine in cystitis, catarrh of the bladder and phosphaturia

**TRAUMATIC PARAPLEGIA** Bladder and rectal functions show a departure from normal and often complete paralysis of micturition. Ammonium benzoate over long periods does not cause digestive upsets like sodium acid phosphate. A routine mixture: Ammonium benzoate 15 gr, hexamine 10 gr, hyoscyamus tincture 30 m, syrup of orange 1 dr, water to 1 oz. The urine can generally be kept at a constant level of acidity by this and drainage. Irrigation with 1 in 8000 potassium permanganate, in some cases. —(C) H. Gotch, *Brit med J*, 1/1923, 849

**P. Mistura Boro-Benzoatis (K C H)**

Ammonium benzoate 20 gr, boric acid 10 gr, tincture of hyoscyamus 30 m, infusion of buchu to 1 oz. A useful urinary antiseptic mixture

**Magnesii Benzoas.**  $(C_6H_5COO)_2Mg=260.4$ 

*Dose* —5 to 15 grains (0.3 to 1 g)

White crystalline powder

**Soluble** 1 in 30 of water, hardly soluble in alcohol 90%

**Incompatible** with acids, also with sodium bicarbonate

Antipyretic. Used as an anti-arthritis for rheumatism and as a cathartic in cirrhosis of the liver

**Potassii Benzoas.**  $C_6H_5COOK, 3H_2O=214.2$ 

*Dose* —5 to 30 grains (0.3 to 2 g)

White crystals. Soluble 1 in  $1\frac{1}{2}$  of water and 1 in 20 of alcohol 90%. Uric acid solvent

**Sodii Benzoas (B P, Fr Cx Supp 1920, P Ital V, U S P XI, P Helv V).**

$C_6H_5COONa=144.0$  *P Ned V* has  $\frac{1}{2}$  mol.  $H_2O$ .

*Dose* —5 to 30 grains (0.3 to 2 g.) *U S P. XI* average dose 15 grains.

In white granular crystals: **soluble** 1 in 2 of cold water and about 1 in 50 of alcohol 90%

Two varieties are made, one from the acid obtained from benzoin, the other from the synthetic acid

**Incompatible** with mineral acids and with ferric salts. It is apt to cause gastric irritation if taken on an empty stomach

**Uses.** Urinary antiseptic. Acute lacunar tonsillitis is stated to be cured by it in 12 to 36 hours if given in 5 to 15 grain doses every 2 hours. In pyelitis due to *B. coli* infection, sodium benzoate combined with hexamine has given good results

**Cryogénine** (*Lumière, I vons, Anglo-French Drug Co., London*) is stated by the makers to be phenyl semicarbazide,  $C_6H_5NHNHCONH_2$  (Other authorities, including *F. L. VIII*, describe it as *m*-benzaminosemicarbazide)

**Dose**—3 to 24 grains (0.2 to 1.5 g.), up to 40 grains (2.5 g.) per day

In white crystals, soluble 1 in 50 of water, 1 in 25 of alcohol 90%. Antipyretic and analgesic for rheumatism, neuralgia, etc. Is valuable for reducing the pyrexia of phthisis and may be given in the afternoon to prevent the evening rise in temperature

### **Benzoinum (B P)**

**Dose.**—10 to 30 grains (0.6 to 2 g.)

The balsamic resin from *Styrax Benzoin* (Sumatra benzoin), containing 19 to 29% of free balsamic acids and not more than 60% of total balsamic acids, calculated on the dry alcohol-soluble matter *U.S.P. XI* allows also Siam benzoin, from *S. tonkinense* or other species *P. Dan* and *P. Helu*. *V* allow Siam benzoin only

**Vap. Benzoin Co. c. Menthol (N I F)**

Menthol 8 gr., benzoin 48 gr., storax 34 gr., balsam of tolu 12 gr., industrial methylated spirit to 1 oz

**Sphygmographic Varnish.** Contains benzoin, balsam of tolu and alcohol. This is used for pulse tracings

### **Tinctura Benzoini Simplex (B P C)**

**Dose.**— $\frac{1}{2}$  to 1 drachm (2 to 4 ml.)

1 in 10 of alcohol 90%. *P. Ital. V* 1 in 5 of alcohol 80%.

One of the tincture in rose water 40, is useful as a face lotion in urticaria and in irritable conditions of the skin

**Tinctura Benzoini (U S P XI)**

**Average dose**—15 minims (1 ml.)

Benzoin (Sumatra or Siam) 1 in 5, in alcohol 95%

### **Lotio Benzoini (B P C) Syn LAITI VIRGINAL**

Tincture of benzoin, 1 in 40, in rose water

### **Nebula Benzoini Composita (B P C)**

Menthol 1% with oils of eucalyptus, cassia and pumilio pine in glycerin and tincture of benzoin.

**Tinctura Benzoini Composita (B.P.) Syn FRIARS' BAL SAM, TRAUMATIC BALSAM.**

**Dose.**— $\frac{1}{2}$  to 1 drachm (2 to 4 ml.)

Benzoin 10%, with storax, aloe and balsam of tolu in alcohol 90%.

A drachm to a pint of hot water is valuable as an inhalation in bronchitis and acute laryngitis. Undiluted it is used as a wound dressing. Is useful internally in chronic bronchitis. Mixtures

require the addition of 1 dr per oz. of mucilage of acacia, or of a mixture of equal parts of mucilages of acacia and tragacanth, to suspend the resins.

**Tinctura Benzoini Composita (U.S.P. XI)**

*Average dose*—30 minims (2 ml)

Benzoin 10, aloë 2, storax 8, tolu 4, in alcohol 95%.

**Collunarium Benzoini (T H)**

Compound tincture of benzoin 5 m, borax 5 gr, water to 1 oz

**Ung. Benzoini et Zinci (C X H)**

Compound tincture of benzoin 2, boric acid ointment 4, zinc ointment 1 olive oil 1

Of value in small ulcers and fissures, especially cracked nipples and small anal fissures Has an anæsthetic and stimulating effect—E C Warner, *Practitioner*, 11/1935, 834

**Benzyl Alcohol.**  $C_6H_5 \cdot CH_2OH = 168.1$

*Dose*—5 to 40 minims (0.3 to 2.5 ml) in water 3 or 4 times a day

A liquid with a slight aromatic odour

Is a satisfactory local anaesthetic, preferably mixed with chloroform A few drops on an exposed nerve or cavity is an efficient anodyne for toothache It is 40 times less toxic than cocaine

**Benzylis Benzoas (B P C, P Dan, F E VIII)**

*Syn and Prop Name* SPASMODIN (Bush, London), ESTER BENCILBENZOICO, PERUSCABINA.  $C_6H_5 \cdot COOC_6H_5 = 212.1$

*Dose*—5 to 8 minims (0.3 to 0.5 ml) as a 1 in 5 alcoholic solution in water, or in capsules, or emulsified with 10% of its weight of powdered tragacanth See also below.

White crystals with faint aromatic odour and burning taste, m.p. 20°, b.p. about 323°. After melting, it may remain liquid at room temperatures, owing to supercooling

**Insoluble** in water and glycerin, miscible with alcohol, chloroform and ether

**Uses.** It is practically non-toxic and has been used in excessive intestinal peristalsis, diarrhoeas and dysentery, intestinal, biliary and renal colic, spastic constipation, vesical spasm, uterine colic, persistent hiccough, arterial spasm and bronchial spasm of true asthma Sometimes of value in whooping-cough but its action is uncertain It has antipyretic action Might be of service in dysmenorrhœa Has been used in lymphatic leucæmia

**Emulsion of Benzyl Benzoate.**

*Dose.*— $\frac{1}{2}$  to 2 drachms (2 to 8 ml) every two hours as required

Benzyl benzoate 1, mucilage of acacia 15, aromatic elixir to 40

Has low toxicity due to conversion into, and excretion as, hippuric acid No serious case of poisoning in many thousands treated. In addition to antispasmodic properties it has antipyretic effect, and is not narcotic even in large doses —D I Macht and H P Leach, *J Pharmacol*, March, 1929, 295

**Benzoylis Peroxidum.**  $C_6H_5 \cdot CO \cdot O_2 \cdot CO \cdot C_6H_5 = 242.1$ . A crystalline compound, m.p. 103.5°, prepared by the interaction of 100 of sodium peroxide and 180 of benzoyl chloride, at a low temperature. Soluble slightly in water, more so in alcohol

**Uses.**—As a dusting powder, as a 2 to 3% solution in oil, or as an ointment in soft paraffin, for burns, ulcers and for dermatitis due to the poison ivy (*Rhus toxicodendron*)

**Benzyl Acetate.**  $\text{CH}_3\text{COOC}_6\text{H}_5 = 150.1$

Only fluid smelling of pears, made from benzyl alcohol, acetic acid and sulphuric acid or by boiling benzyl chloride with alcoholic potassium acetate

**Benzylis Succinas (B P C)** *Prop Name* SPASMINE (*Bush, London*)

$(\text{CH}_2\cdot\text{COOCH}_2\text{C}_6\text{H}_5)_2 = 298.1$

*Dose* —5 to 15 grains (0.3 to 1 g.) in tablets or capsules

This is a tasteless crystalline substance, **soluble** in alcohol, ether, chloroform, and fixed and volatile oils, almost insoluble in water. Not nauseating to the stomach. It is employed for conditions similar to those for which the benzoate has been given.

[P 81] **Capsules of benzyl succinate** 5 grains with papaverine sulphate  $\frac{1}{2}$  grain (sometimes also with hyoscyamine) are prepared for the combined effect of these bodies.

[P 81] **Spasticine** (*Napp, London*) Tablets, containing benzyl succinate 0.3 g., papaverine hydrochloride 0.03 g., atropine methylbromide 0.0005 g.

*Dose* —From 1 to 3 tablets three times a day. Antispasmodic.

**Acidum Hippuricum.** *Syn* BENZAMINO-ACETIC ACID, BENZOYL GLYCOCOLL  $\text{C}_6\text{H}_5\text{CONHCH}_2\text{COOH} = 179.1$ .

*Dose* —5 to 20 grains (0.3 to 1.2 g.)

This acid, occurring as white crystals, **soluble** in hot water (very slightly in cold—about 1 in 600), melting at  $187^\circ$ , may be prepared from the urine of herbivora, also synthetically by treating glycocoll (aminoacetic acid,  $\text{CH}_2\text{NH}_2\text{COOH}$ , *qv*) with benzoyl chloride or benzoic anhydride.

**Ammonii Hippuras (B P C)**  $\text{C}_9\text{H}_8\text{O}_3\text{N}(\text{NH}_4) = 196.1$

*Dose* —5 to 20 grains (0.3 to 1.2 g.)

Small white or brownish-white crystals. **Soluble** in water, and 1 in 20 of alcohol 90%. This and other hippurates have been given in gouty conditions. They are also administered, with other substances, in the treatment of arterial hypertension.

Sodium, potassium and calcium hippurates are salts with properties allied to those of the ammonium compound.

**Acidum Mandelicum.** *Syn*  $\alpha$ -HYDROXYPHENYLACETIC ACID  $\text{C}_6\text{H}_5\text{CHOHCOOH} = 152.1$

*Dose* —45 grains (3 g.) in 1 oz. of water, neutralised with sodium bicarbonate, four times a day.

In white crystals with acid taste. M.p. about  $119^\circ$ . Obtained from benzaldehyde by treatment with potassium cyanide and hydrolysis of the resulting cyanohydrin.

**Soluble** 1 in about 8 of water, 1 in 2 of alcohol.

**Contraindications.** Mandelic acid should not be given when there is impairment of renal function.

**Uses.** Introduced to replace the ketogenic diet in the treatment of urinary infections. The bacteriostatic substance in urine of patients on ketogenic diet is  $\beta$ -hydroxybutyric acid. If the acid is given orally it has been found to be almost completely oxidised in the body (but *vide infra*). Mandelic acid was selected, after trial of other hydroxy acids, as being least toxic, most

effective and at the same time easily obtained. Its bacteriostatic action is only exerted when the urine is not less acid than pH 5.5, and the acidity of the urine is maintained by the simultaneous administration of ammonium chloride.

**Rosenheim's Routine.** 12 g of mandelic acid is given daily in divided doses, the fluid intake being limited to 2 pints daily. The standard mixture contains 45 gr (3 g) of acid per oz of water, just neutralised with sodium bicarbonate 24 gr (1.6 g), and flavoured with lemon, 1 oz is given four times a day. 8 cachets, each containing 15 gr (1 g) of ammonium chloride, are given during the day. The urinary pH must be controlled by tests with methyl red (the colour produced should be reddish-orange but not yellow, the test is best carried out on the early morning urine).

A preliminary report on the above treatment. Of 12 cases of cystitis, pyelitis or pyclitis of pregnancy, in whom the duration of infection varied from 1 week to about a year, clinical improvement or cure was noted in 10, and the urine became sterile in 4 and much reduced in bacterial content in 4. Of 6 cases of urinary infection unassociated with pregnancy all were improved and 3 cured. In 2 cases of pyelitis of pregnancy no improvement either bacteriological or clinical was observed. There was no evidence of renal irritation although casts were found in 2 cases (in 1 probably not due to the acid). Some buzzing in the ears and temporary deafness occurred in two or three patients, but no other complications.—M. L. Rosenheim, *Lancet*, 1/1935, 1032. See also *ibid*, 11, 1935, 741.

A report on 16 cases of urinary infection treated with mandelic acid prescribed in the form of a neutral mixture as follows: mandelic acid, 45 grains, sodium bicarbonate, 21 grains, syrup aurant, 1 drachm, water to 1 ounce. Dose—1 ounce 4 times daily in water. Taken together with sufficient dosage of ammonium chloride to maintain a primary pH below 5.5, 6 ten-grain cachets a day usually being sufficient. Fluid intake limited to between 2 and 3 pints a day. With three exceptions the treatment sterilised the urine in from 5 to 12 days. A striking feature of the treatment was the diminished frequency of micturition and diminished dysuria. Only trivial side-effects (slight giddiness, buzzing in the ears) were observed.—D. M. Lyon and D. M. Dunlop, *Brit med J*, 11/1935, 1096.

Toxic symptoms following treatment—severe aching of neck and leg muscles together with urticarial rash. Symptoms disappeared on discontinuance of drug.—S. Chaplin, *ibid*, 1100.

The effect of mandelic acid on bacteria in the urine depends upon the nature of the infecting organism, the concentration of mandelic acid and the acidity of the urine. As the acidity of the urine increases the concentration of mandelic acid required decreases. *Escherichia coli* is killed by 0.25% of mandelic acid at pH 5 but requires 1% at pH 5.7. *Proteus ammoniae* is also destroyed by 1% at pH 5.7 but with 0.25% a pH of 5.3 is necessary. *Aerobacter* sp. and *Pseudomonas* sp. are more resistant, requiring 0.5% at pH 5 and 1% at pH 5.3.—H. F. Helmholz and A. E. Osterberg, *Proc Mayo Clin*, 1936, 373.

**Neoket (Boots, Nottingham).** Compound effervescent granules of mandelic acid. Contains in 2 teaspoonfuls (90 gr) mandelic acid 45 gr, sodium bicarbonate 25 gr, sodium acid phosphate 30 gr, soluble saccharin  $\frac{1}{2}$  gr, flavouring oils q s.

Dose.—Two teaspoonfuls in water four times daily immediately after each meal.

In some cases the optimum urinary pH can only be attained with the supplementary administration of ammonium chloride.

**Sodii Mandelas.**  $C_6H_5 \cdot CHOH \cdot COONa$  = 174.1

Dose.—50 grains (3.4 g) four times daily, with supplementary treatment as with mandelic acid.

In white crystals with faintly aromatic odour **Soluble** 1 in about  $1\frac{1}{2}$  of water, almost insoluble in cold alcohol 90%

A convenient form for administering the acid

Successful clinical results with sodium mandelate given in a mixture containing sodium mandelate 50 gr, syrup of orange 1 dr, water to 1 oz To be taken 4 times a day in water, each dose to be preceded by the requisite dose of a mixture containing ammonium chloride 30 gr, liquid extract of liquorice 15 m, water to 1 oz The dose of ammonium chloride must be adjusted to give a urinary pH of 5.3 or less (pink with methyl red) No deleterious effects in nephritis or nephrosis.—H. E. Holling and R. Platt, *Lancet*, 1/1936, 769

**Ammonii Mandelas.**  $C_6H_5 \cdot CHO \cdot COONH_4 = 169.1$ .

**Dose.**—50 grains (3.4 g) four times daily in aqueous solution.

White very hygroscopic needles, very easily soluble in water and alcohol. Suggested to replace sodium mandelate and ammonium chloride, the ammonium radicle being converted in the body to urea and the mandelic acid radicle serving to acidify the urine. The nausea and vomiting sometimes caused by ammonium chloride are thus avoided. Sometimes ammonium chloride must also be given to obtain the necessary acidity. More rarely an excessively acid urine is obtained and in these cases some sodium bicarbonate must be given.

Ammonium mandelate found as effective as the sodium salt in the treatment of urinary infections and usually obviated the necessity of giving the unpleasant ammonium chloride.—H. E. Holling and R. Platt, *Lancet*, 1/1936, 771

The following is a much-used formula readily made in the dispensary—Mandelic acid 36 g, strong solution of ammonia 264 m, liquid extract of liquorice 240 m, tincture of ginger 20 m, tincture of capsicum 20 m, syrup 1 oz, mucilage of ceratonia 3 oz, chloroform water to 12 oz 1 oz of this mixture contains  $\frac{1}{2}$  g of mandelic acid as ammonium mandelate, and, taken with an equal amount of water, is the usual adult dose. When the solution of ammonia is added to the acid in a bottle, a syrupy solution of ammonium mandelate is formed almost immediately. It is convenient to keep this solution ready as a "stock" solution, each 55 m representing 3 g of acid. The colloid gum, by retarding absorption in the mouth, makes the mixture less unpalatable. The concentrated "stock" solution may be put up in capsules, which are rendered insoluble by exposing them, separated bottom from cap, in a bottle overnight with a paraform tablet. The dose can be contained in four of these capsules. The capsules keep at least a week, but probably not indefinitely.—W. A. Knight, *Pharm J*, 11/1936, 250.

**Ammoket** (*Boots, Nottingham*) Elixir of ammonium mandelate containing ammonium mandelate 52 gr, elixir of saccharin 5 m, liquid extract of liquorice 5 m, sucrose 110 gr, spirit of chloroform  $7\frac{1}{2}$  m, essential oils q s, water to  $\frac{1}{2}$  oz.

**Mandelix** (*British Drug Houses, London*) Elixir of ammonium mandelate containing the equivalent of 45 gr (3 g) of mandelic acid in 2 dr. Complete outfits are available containing the elixir, cachets of ammonium chloride and a testing outfit for determining the urinary pH.

**Mist. Ammon. Mandelat. Co.** (*Martindale, London*) is a lemon-flavoured preparation containing ammonium mandelate equivalent to 45 gr of mandelic acid and 25 gr. of sodium acid phosphate in  $\frac{1}{2}$  oz.

**$\beta$ -Hydroxybutyric Acid.**

The bacteriostatic action of the urine of patients taking the ketogenic diet (see Vol II) is due to the presence of *l*- $\beta$ -hydroxybutyric acid. When given orally in 1 g doses three times daily only a small increase in the output of the acid in the urine was obtained.—A. T. Fuller, *Lancet*, 1/1933, 855.

Theoretically  $\beta$ -hydroxybutyric acid would be completely burned if the body were in a normal metabolic state. If an individual is already in a state of ketosis so that the acid is present in amount in excess of what the body can oxidise, oral administration should increase the amount excreted by the kidneys. The administration of 2 g of the acid as the sodium salt orally, three times daily, may be useful as an adjunct to the ketogenic diet in those cases where the diet

alone does not produce a sufficiently bactericidal urine—E N Cook, *Proc Mayo Clin*, 1936, 310

**Acidum Cinnamicum.** *Syn* PHENYLACRYLIC ACID, CINNAMYLIC ACID  $C_6H_5 \cdot CH \cdot CH \cdot COOH = 148.1$

*Dose.*—2 to 3 grains (0.12 to 0.2 g) by mouth,  $\frac{1}{4}$  to  $\frac{1}{2}$  grain (0.0013 to 0.02 g) by hypodermic injection, in oily solution

Made by oxidising cinnamon oil or by acting upon benzaldehyde with acetyl chloride. Transparent micaceous crystals, m.p. 132° to 135°, slightly soluble in water, soluble in alcohol, ether and oils. Has been used to induce leucocytosis. Mostly given as the sodium salt

**Sodii Cinnamas.**  $C_6H_5 \cdot CH \cdot CH \cdot COONa = 169.1$

*Dose.*—2 to 5 grains (0.12 to 0.3 g)

A white crystalline powder with faint aromatic odour. **Soluble** 1 in 11 of water, 1 in 10 of glycerin, 1 in 160 of alcohol 90%. Has been administered orally or hypodermically in the treatment of tuberculosis

**Glycerinum Sodii Cinnamatis.**

*Dose.*—30 to 60 minims (2 to 4 ml), by injection. A 10% solution in glycerin, made by heating to not exceeding 180°. Has been used hypodermically and intravenously in tuberculosis and cancer, it causes a general leucocytosis

**Strontil Cinnamas.**  $(C_6H_5 \cdot CH \cdot CH \cdot COO)_2Sr = 381.7$

*Dose.*—2 to 5 grains (0.12 to 0.3 g). A white powder, soluble about 1 in 120 of water and about 1 in 50 of a mixture of glycerin and water equal parts, and about 1 in 100 of alcohol 90%. This has been used similarly to the sodium salt

**Thermiol** (*Schuchardt, Görlitz*). A 25% aqueous solution of sodium phenylpropionate,  $C_6H_5 \cdot C \cdot C \cdot COONa$

Has been used in laryngeal and pulmonary tuberculosis by inhalation of 0.5 to 3% solutions

**Cinnaldehydum.** *Syn* CINNAMAL (*P Austr*)

$C_6H_5 \cdot CH \cdot CH \cdot CHO = 132.1$

*Dose.*—1 minim

The aldehyde occurring in cinnamon oil. A colourless liquid with cinnamon odour. Sp. gr. 1.054 to 1.056. **Soluble** in alcohol in all proportions

**Capsules** (*Gelatin*), 1 minim, have been used in malignant disease and in tuberculosis, especially in pulmonary cases

**Cinnoxyl Capsules** (*Comar, Paris*) are stated to contain benzyl cinnamate,  $C_6H_5 \cdot CH \cdot CH \cdot COOC_7H_{15} = 238.1$ , and cholesterol

**Jacobson's Solution** (*Boots, Nottingham*) *Syn* BENZYL CINNAMIC ESTER

A solution of ethyl cinnamate,  $C_6H_5 \cdot O_2 \cdot C_2H_5$ , in benzyl alcohol and olive oil

*Dose.*—0.25 to 1 ml intramuscularly in the gluteal muscles

In tuberculosis, both glandular and pulmonary, lupus, salpingitis and trachoma. Contraindicated in nephritis

Improvement in all cases. 0.25 ml intramuscularly daily for 12 days, followed by rest of 15 days, and after three series a rest of 1 month—H Gainsborough, *Lancet*, 1/1928, 906 and with P. J Joy *Lancet* 1/1929, 1142. In "external" and general tuberculosis *Lancet*, 1/1929, 320

**Acidum Coumaricum.** *Syn* o-HYDROXYCINNAMIC ACID

$C_6H_4(OH) \cdot CH \cdot CH \cdot COOH = 164.1$

Brownish crystals, m.p. 200°. The *meta*- acid melts at 191°, and the *para*- at 206°. The use of this hydroxy compound (as



sodium salt) was a step forward from cinnamic acid as an excitant of leucocytosis.

**Soluble** very slightly in chloroform, in alcohol 1 in 12 or less, in ether 1 in 36, hardly soluble in water. The coumarates have action of vasodilators, and they may be taken for prolonged periods without harm

**Injectio Sodii o-Coumaratis.** A 22% aqueous solution of sodium o-coumarate,  $C_9H_7O_3Na$ . Has been used in cancer and tuberculosis

**Dose**—25 minims (1.5 ml), thrice weekly when possible between the growth and healthy subjacent tissues or in the course of lymphatics proceeding from the region of the growth, or over a large serous sac like the peritoneum. In glandular and early cases of pulmonary tuberculosis Drage reported good results. In cancer he held that few drugs exert more definite action

**Tylmarin** (*Martindale, London*) **ACIDUM ACETYLI -o-COUMARICUM**  
 $CH_3COO C_6H_4 CH CH COOH = 206.1$

**Dose**—5 to 10 grains thrice daily after food. Colourless crystals, m.p.,  $150^\circ$ . **Soluble** slightly in water, in alcohol 90% 1 in 19. In tuberculosis and as a general intestinal antiseptic. Tylmarin Dusting Powder has been used for cancerous growths which have broken down. Large open sores can be materially benefited

The sodium, quinine and thorium salts are also available

**Coumarin.** *Syn* COUMARIC ANHYDRIDE  $C_9H_6O_2 = 146.05$

The lactone of coumaric acid. In colourless crystals with aromatic odour and taste, contained in tonquin beans, also in woodruff. It is made synthetically by boiling salicylic aldehyde with acetic anhydride and sodium acetate

**Soluble** in alcohol, ether and oils, but not to any extent in water. Sublimes unchanged. One part will disguise the odour of 50 of iodoform

**Tonco Semen** (*B.P.C.*) *Syn* TONKA or TONQUIN BEANS

The seeds of *Dipteryx odorata* and of *D. oppositifolia* (*Leguminosæ*), dried in the sun or cured by immersion in rum for a few days and drying. Formerly used as a source of coumarin; also used in perfumery

**Vanilla** (*B.P.C.*) consists of the cured capsular fruits of *V. planifolia* (*Orchidaceæ*). Contains 2 to 3% of vanillin and other unknown aromatic substances

**Vanillinum** (*B.P.C., U.S.P. XI, P. Helv. V*)

*Syn* VANILLIC ALDEHYDE, METHYLPROIOCAATECHUIC ALDEHYDE, METHOXYBENZALDEHYDE.  $CH_3O C_6H_4(OH) CHO = 152.1$

White crystalline needles with intense vanilla odour and taste. Can be extracted from vanilla, but is usually prepared synthetically from eugenol

**Soluble** in most organic solvents, slightly soluble in water, more soluble in hot water; readily soluble in alkalis.

Use suggested in atonic dyspepsia as an excito-motor stimulant. For employment in Gunzburg's test, *vide Vol. II. Solutio Vanillini*—Vanillin 80 gr, alcohol 90% to 1 oz. For ordinary purposes  $\frac{1}{2}$  dr will flavour a pint of medicine. **Essence of Vanilla** 1 in 8 by macerating vanilla beans 1 finely ground with sand 1, in a mixture of water 2, and alcohol 90% 6

**Elixir Vanillini Compositum** (*N.F. VI*). *Dose*.— $\frac{1}{4}$  to 1 drachm. Mix compound spirit of vanillin 20, with 95% alcohol 80, add glycerin 25, then syrup 300, caramel 2, and water to 1000 F 'ter

**Spiritus Vanillini Compositus** (*N.F. VI*). *Dose*.— $\frac{1}{4}$  to 1 drachm. Vanillin 40, oil of orange 10, oil of cardamom 2, oil of cinnamon 1, are dissolved in a sufficiency of alcohol 95% to make 200

**Agaricus** (*B.P.C.*). *Syn* POLYPORUS OFFICINALIS, BOLETUS LARICIS, FUNGUS LARICIS (*P. Austr.*, *P. Ital. V*), POLYPORUS DE MÉLÈZE (*Fr. Cx*), PURGING AGARIC

*Dose*.—3 to 30 grains.

The dried fungus *Fomes officinalis*, in light, spongy pieces. Large doses purgative, small ones astringent for night sweats, diarrhoea and to diminish bronchial secretion. *Tincture*, *dose*.—20 to 60 minims, 1 in 10 of 60% alcohol. *Extract*, *dose*.— $\frac{1}{4}$  to 2 grains, prepared by exhaustion with 60% alcohol, about 6°.

**Acidum Agaricum** (*B.P.C.*, *P.G. VI*, *P. Ital. V*, *P. Helv. V*, *P. Jap.*, *P. Dan.*). *Syn* AGARICIN, LARICIC ACID

$\text{CH}_2\text{C}(\text{OH})\text{CH}(\text{C}_{16}\text{H}_{33})\text{COOH}$ ,  $1\frac{1}{2}\text{H}_2\text{O} = 443.3$

*Dose*.— $\frac{1}{2}$  to  $\frac{1}{4}$  grain (0.005 to 0.03 g). *P.G. VI*, *P. Helv. V* and *P. Ital. V* have max. single dose  $1\frac{1}{2}$  gr.

Obtained from the fungus, *Fomes officinalis*, growing on larch trees. An odourless, tasteless microcrystalline powder, **soluble** 1 in 130 of water. Given to restrain the night sweats of phthisis. Owing to slow absorption should be given some hours before retiring.

**Amadou**. *Syn* OAK AGARIC, SURGEON'S AGARIC, LARCHWOOD *Polyporus fomentarius* L. A fungus prepared with alkali and nitre, in light brown elastic pieces. Employed as a mechanical hæmostatic. It is included in *P. Austr.* under the name *Fungus ignarius*.

## ACIDUM BORICUM

*B.P.*, *U.S.P. XI*, *P. Helv. V*, *P. Dan.*, *P. Belg. IV*, etc.

*Syn* BORACIC ACID, HYDROGEN BORATE, SAL SEDATIVA DE HOMBERG (*F.E. VIII*)

$\text{H}_2\text{BO}_3 = 61.84$

*Dose*.—5 to 15 grains (0.3 to 1 g).

Made by the action of sulphuric acid on borax and other borates. In white laminar crystals, with bitter taste, or as powder (that known as Pulv. Acid. Boric. Subtilis has been passed through a No. 170 sieve). The crystals yield a clearer solution than the powder.

**Soluble** 1 in about 25 of water, 1 in 3 of boiling water, 1 in 30 of 90% alcohol, 1 in 5 of glycerin at 0°, 7 in 10 at 100°, slightly soluble in volatile oils. Insoluble in ether.

**Antidotes**. Empty stomach by stomach tube or emetic. Give purgative dose of magnesium sulphate.

A teaspoonful taken in error has caused death. Used for lavage, it may prove poisonous owing to idiosyncrasy, producing a rash.

Fifty per cent. of the acid administered is excreted in the urine within 12 hours, the rest remains in the body for 3 to 4 days and hence may accumulate under repeated dosage.

Fatal poisoning of babies each weighing about 7 lbs. with from 0.8 to 3 g. of boric acid given in solution in error for water—*Pharm. J.*, 1/1927, 361.

**Uses.** Antiputrefactive and mildly antiseptic. Has been given as antiseptic before and after bladder operations, in typhoid, and also for cystitis. It is used as a dressing to wounds, sores, and the skin generally. When mixed with starch, with or without zinc oxide, it forms a useful "dusting powder" for infants, etc. A little in the socks or stockings prevents the odour of perspiring feet.

Vomiting in gastric dilatation or gastric catarrh of infants has been treated by washing out the stomach with weak boric acid lotion. In otorrhœa an alcoholic solution of boric acid may be used.

### **A.B.C. Powder.**

Boric acid, bismuth subnitrate and calomel, equal parts. A stimulant antiseptic dusting powder.

**Carbasus Acidi Borici (B.P.C.)** *Syn.* BORIC GAUZE

Contains 10 to 20% of boric acid

**Cataplasma Acidi Borici (B.P.C.)**. 20% in linseed poultice

**Cataplasma Acidi Borici et Carbonis (B.P.C.)** 4% of each in slippery elm poultice

**Cataplasma Amyli et Acidi Borici (B.P.C.)** Boric acid 6% in starch poultice

**Collyrium Acidi Borici (B.P.C.)** 2% w/v.

**Collyrium Acidi Borici et Zinci (B.P.C.)** Contains 4 gr of boric acid and 1 gr. of zinc sulphate per oz

**Glycerinum Acidi Borici (B.P.)**

*Syn.* GLYCERITE OF BOROGLYCERIN (*U.S.P. XI*)

*Dose.*—10 to 30 minims (0.6 to 2 ml)

Consists of glyceryl borate and glycerin, and contains the equivalent of 31% w/w of boric acid

It is readily miscible with water and alcohol. Of value in otorrhœa

**Boroglycerinum (B.P.C.)** is a similar preparation containing the equivalent of 50% w/w of boric acid

**Gossypium Acidi Borici (B.P.C.)** *Syn.* BORIC WOOL

Contains 15 to 30% of boric acid

**Gutt. Auribus Boric. (N.I.F.)**

Boric acid 35 gr, industrial methylated spirit 77 m, glycerin to 1 oz

**Lintum Acidi Borici (B.P.C.)** *Syn.* BORIC (BORACIC) LINI

Contains 35 to 45% of boric acid

**EPIDERMOPHYTOSIS** Trichophyton infection (interdigital) cured by insertion of small strips of boric lint, about 1 inch by  $\frac{1}{4}$  inch, well pressed into the affected spaces and renewed night and morning. This ensures relative dryness and inhibits growth of the mould. —*Brit. med. J.*, 11/1934, 889.

**Lotio Acidi Borici (B.P.C.)** 1 in 30

A useful soothing antiseptic lotion for the eyes, bladder, vagina and mouth.

**Lotio Acidi Borici (R.L.O.H.)** 8 gr to 1 oz (2% approx)

**Isotonic Boric Acid Lotion** is 3.1% strength—isotonic with the tears

**Lotio Acidi Borici cum Zinci Sulphatis (R.L.O.H.)**

Boric acid 8 gr., zinc sulphate  $\frac{1}{2}$ , 1 or 2 gr, water to 1 oz

**Oculentum Acidi Borici (B.P.C.)**. 4% in simple eye ointment

**Oculentum Acid. Boric. (N.I.F.)**

Boric acid  $2\frac{1}{2}$  gr, white soft paraffin to 1 dr

**Pastillus Acidi Borici (T.H.), v** Glyco-gelatin Pastilles

Useful in aphthous affections of the mouth and throat

**Pessus Acidi Borici (B.P.C.)** contain 10 gr (0.6 g)

Convenient to replace douches after delivery

**Pessus Glycerini Acidi Borici** for vaginal use weigh 90 gr each, and contain 70 gr of glycerin of boric acid with gelatin 10 gr and water 10 m

**Pulvis Talci Boricus (B.P.C.)** Boric acid and starch, of each 10%, with purified talc, perfumed with oil of geranium

**Solvellæ Acidi Borici (B.P.C.)** contain 15 gr (1 g)

**Suppositorium Acidi Borici** contains 3 gr (0.2 g) in each Useful in pruritus

**Unguentum Acidi Borici (B.P.)** Boric acid 1, white paraffin ointment 9 This ointment is much softer than that of the B.P. '14 The following formulæ were proposed by Martindale—

	No 1	No 2	No 3
Paraffin (m.p. 57°)	5	5	5
White Soft Paraffin	5	10	15
Boric Acid, in fine powder	2	3	4

Melt the paraffins, sift the boric acid into the liquid, and stir constantly till cold These three ointments contain the same quantity of boric acid, i.e., 1 to 5 of basis.

"No. 1" is used where cavities exist or where a stiff base is needed. "No. 2" is for surface wounds, burns, eczema, chaps, pruritus ani et pudendi, and sores, as an antiseptic dressing and "healing ointment" "No. 3" is for toilet use

**Unguentum Acidi Borici (U.S.P. XI)**

Boric acid 10, wool fat 5, white wax 5, white petrolatum 80

**Unguentum Acidi Borici Flavum (B.P.C. and N.I.F.)** 10% in yellow soft paraffin

**Unguentum Lano-Boricum Camphoratum.**

Boric acid ointment (No. 2)  $\frac{1}{2}$  oz, hydrous wool fat  $\frac{1}{2}$  oz, essential oil of camphor 20 m

For earache in children Applied with a brush to the meatus

**Borax (B.P., P. Helv. V., P. Dan.)** Syn. SODII BORAS (U.S.P. XI), SODIUM BORATE, BIBORATE, PYROBORATE or TETRABORATE  $\text{Na}_2\text{B}_4\text{O}_7 \cdot 10\text{H}_2\text{O} = 381.4$ .

**Dose**—5 to 15 grains (0.3 to 1 g)

**Soluble** 1 in 25 of water, 1 in 1 of glycerin, insoluble in alcohol 90%.

**Incompatible** with cocaine hydrochloride, mercuric chloride, zinc sulphate, and other metallic salts. In these cases all incompatibility may usually be overcome by the addition of glycerin or by replacing half the borax with boric acid. Also incompatible with gums and mineral acids.

**Uses.** As gargle in diphtheria for aphthæ, cancrum oris, and gangrenous stomatitis. As lotion in pruritus ani and vulvæ, in bromidrosis and fœtid sweating of the feet. Gouty affections are treated with compresses of saturated solution.

Internally is frequently included in bromide mixtures as a sedative and for epilepsy.

**EPILEPSY**—Better than Luminal. Treatment consists essentially of borax 10 gr and sodium bromide 10 to 15 gr thrice daily. If the fits do not cease in a fortnight, the borax is increased to 15 gr. After 6 weeks 15 minims of belladonna tincture daily are given in addition if necessary, and after 2 months it is reduced and then omitted. The salt mixture is given for a year at least, when the bromide is gradually reduced. The patient then remains on borax for another year. This almost invariably achieves a cessation of fits in adults, but children do not as a rule respond so well.—P. Figdor, *Lancet*, 11/1925, 840, 892, 943.

**HYPERTHYROIDISM**—A daily dose of 2 to 4 ml of a 5% solution of sodium borate taken with meals gave good results.—*J. Amer. med. Ass.*, 11/1925, 308.

**Collyrium Boracis (B.P.C.)** 1% w/γ

**Gargarisma Boracis (B.P.C.)** Borax 15 gr per fl oz

**Glycerinum Boracis (B.P.)**

Borax 12% w/w in glycerin. Has an acid reaction and liberates carbon dioxide from carbonates. Is useful in infantile diarrhœa in 20 m doses.

**Fatal poisoning** in two-weeks-old child following ingestion of 1½ drachms of borax and boric acid in the form of honey and borax and glycerin of borax a dummy teat dipped in the latter may convey 1½ to 2 grains of borax to the child's mouth.—*J. Birch, Brit. med. J.*, 1/1928, 177, *Lancet*, 1/1928, 287.

**Liquor Alkalinus (B.P.C.)** *Syn* COLLUNARIUM ALKALINUM.

Borax and sodium bicarbonate 1 in 80 of each, with phenol and sucrose, in water.

**Liquor Boracis Compositus (B.P.C.)** *Syn* DOBELL'S SOLUTION, COLLUNARIUM ACIDI CARBOLICI COMPOSITUM.

Borax and sodium bicarbonate 1 in 80 of each, with phenol, glycerin and water.

**Mel Boracis (B.P.).** *Syn* BORAX HONEY, BORAX AND HONEY.

Borax 10% w/w in glycerin and purified honey.

**Pulvis Boracis Compositus (B.P.C.)** *Syn* PULVIS ALKALINUS COMPOSITUS.

Equal parts of borax, sodium bicarbonate and sodium chloride.

**Pulvis Sodii Chloridi Compositus (B.P.C.)**

Equal parts of borax, sodium bicarbonate, sodium chloride and sucrose.

**Solvellæ Antisepticæ (B.P.C.).** *Syn* EFFERVESCENT MOUTH-WASH TABLETS.

Contain 3 gr of borax with sodium benzoate, menthol, and other aromatics in an effervescing basis

**Solvellæ Boracis Compositæ (B P C)**

Contain borax 5 gr, sodium chloride and sodium bicarbonate of each  $2\frac{1}{2}$  gr, thymol  $\frac{1}{10}$  gr

**[P1] Solvellæ Boracis et Benzaminæ Compositæ (B P C)**

*Syn* NASO-PHARYNGEAL SOLUTION-TABLETS

Contain borax 3 gr, benzamine hydrochloride  $\frac{1}{2}$  gr, with sodium chloride, sodium benzoate, menthol, thymol and oil of sweet birch.

**[D P1 81] Solvellæ Boracis et Cocainæ Compositæ (B P C)**

Contain sodium chloride 5 gr, borax 3 gr, and cocaine hydrochloride  $\frac{1}{2}$  gr, with sodium benzoate, boric acid, menthol, thymol and oil of sweet birch

**Sodii Boro-Tartras.** *Syn* TARTARUS BORAXATUS

*Dose*—20 to 40 grains (1.2 to 2.5 g)

Borax 2, potassium acid tartrate 7, water 15, evaporate until a little of the residue cooled is brittle. Powder and dry at 50°. Antiseptic and diuretic.

**Potassii Biboras.** *Syn* POTASSIUM PYROBORATE  $K_2B_4O_7 \cdot 5H_2O = 323.6$

Prismatic crystals, readily soluble in water

Variouse and traumatic ulcers treated with tri-weekly application consisting of boric acid 63 g, potassium hydroxide 28 g, water 200 ml, starting with half-strength solution -- *Per J trop Med (Hvg)*, 1926, 165

**Sodii Perboras (B P C, F, Cx Supp 1926, FE VIII, U S P XI)**  $NaBO_3 \cdot 4H_2O$  153.98

*Dose*—U S P XI gives average dose 1 grain (0.06 g)

A white permanent powder **Soluble** in water, about 1 in 40, with decomposition, giving an alkaline solution containing free hydrogen peroxide. Is more soluble in solutions of boric, tartaric or citric acids, and in glycerin

Sodium perborate may be prepared pure by treating crystalline borax 380 g with normal sodium hydroxide 2000 ml to convert it into sodium metaborate,  $NaBO_2$ , and then adding to the solution 4500 ml of 10 volume hydrogen peroxide solution. Cool immediately by refrigeration and collect and dry the crystalline precipitate on filter paper

**Uses.** Antiseptic and deodorising

To produce oxygenated water, 1 kilo yields 104 g, or about 72 litres of active oxygen. This quantity will produce 7 to 7.5 litres of "10 volume" oxygenated water. The solution is not acid. It contains hydrogen peroxide and borax. In practice, 170 g, with 60 g of citric acid makes a litre of about "10 volume" strength. These solutions may be used to prepare antiseptic lotions, vaginal injections (about "5 volume" strength), e.g., in leucorrhœa and metritis, and are useful in minor surgery. The dry salt may be used as a disinfectant, deodorant dusting powder. It has been used for soil-contaminated wounds

Tonsillitis occurring as complication in typhoid has been treated with sodium perborate gargle, 2 dr to the pint

**PARONYCHIA** -- Make a paste with sodium perborate and water. Gently work this in under the nail-fold with a cotton-tipped toothpick and also pack round

the sides and under the nail. Draw on a rubber finger-cot and allow to remain overnight. The infected finger is then soaked three times a day in a warm solution of sodium perborate made by adding two teaspoonfuls to half a glass of water, and continue soaking as long as effervescence takes place. Cases usually cured in 3 to 8 weeks.—E. M. Rockwood, *New Engl J Med*, 1/1933, 295.

VINCENT'S ANGINA.—Rapid cure in 95% of cases with 2% sodium perborate solution as a mouth wash. Best used as a thick paste and retained in the mouth for 4 or 5 minutes while oxidising froth develops.—*J Amer med Ass*, 11/1928, 247.

**Unguentum Sodii Perboratis.** 1% in paraffin ointment basis. Antiseptic and healing.

**Sodium Perborate Tooth Powder.** Sodium perborate 2%, in precipitated calcium carbonate.

There is no carefully controlled evidence that sodium perborate is beneficial to the gums, that it bleaches the teeth or that its use prevents diseases of the gums. Unless the powder and the alkali resulting from its decomposition be thoroughly removed, inflammation and necrosis of the oral membrane may result.—Rep. of Council on Dental Therapeutics of the American Dental Association, per *Pharm J*, 11/1935, 600.

**Calcii Perboras.** A bulky powder less stable than sodium perborate. Has been used in tooth powders.

**Magnesii Perboras** is similar.

**Magnesii Borocitras (B.P.C.)**

*Dose* —15 to 30 grains (1 to 2 g.)

**Manufacture.** Dissolve light magnesium carbonate 70 in a solution of citric acid 100 in water 400, add boric acid 30, evaporate to dryness on a water bath and powder or scale.

The *B.P.C.* gives method of preparation from magnesium oxide.

A white powder or colourless scales, readily soluble in water, used as a urinary antiseptic internally for stone, gout, and rheumatism.

**Pulvis Magnesii Borocitratis Compositus (B.P.C.)** *Syn* BORACITE.

*Dose* — $\frac{1}{2}$  to 1 drachm (2 to 4 g.)

Magnesium borocitrate 1, sucrose 2.

## ACIDUM CITRICUM

*B.P., U.S.P. XI, P. Dan., P. Helv. V, etc*

$C_3H_4OH \cdot (COOH)_3 \cdot H_2O = 210.1.$

*Dose* —5 to 30 grains (0.3 to 2 g.)

Colourless crystals or white powder, obtained from lemon juice, which contains as much as 7 to 9% (30 to 40 gr per oz), or prepared synthetically from glucose.

**Soluble.** 2 in 1 of water, 1 in 2 of glycerin, 1 in 1½ of alcohol (90%), 1 in 8 of ether of sp. gr. 0.735, but much less soluble in 0.720 ether.

**Incompatible** with potassium tartrate and alkaline carbonates.

**Uses.** In dilute solution relieves thirst in fever. For other purposes is usually administered as alkali citrate.

**Collutorium Acidii Citrici (R.D.H.).**

Citric acid 10 gr., solution of formaldehyde 1 m., water to 1 oz. To be used on the tooth brush with an equal quantity of water.

[P2] **Lotio Acidi Citrici et Phenolis.**

Citric acid 3 dr, phenol  $\frac{1}{4}$  oz, water to 20 oz. For cleansing sockets after removing septic teeth

**Potassii Citras** (*B.P., U.S.P. XI, P. Dan.*)

$\text{COOK} \cdot \text{C}(\text{OH})(\text{CH}_2 \text{COOK})_2 \cdot \text{H}_2\text{O} = 324.4$

*Dose.*—15 to 60 grains (1 to 4 g.) *U.S.P. XI* average dose 15 grains.

White granular crystals obtained from citric acid and potassium carbonate

**Uses.** It has diaphoretic, diuretic, and febrifuge properties. Is excreted as carbonate, rendering the urine alkaline, and is therefore given in cystitis, gout, and enuresis where the urine is over-acid. Large doses are useful for the acidæmia of diabetes. Is expectorant in the early stages of bronchitis and tracheitis with viscid, scanty secretion.

**Potassii Citras Effervescens** (*B.P.C.*) About 1 in 6

*Dose.*—1 to 2 drachms (4 to 8 g.)

**Potassii Citras Effervescens** (*U.S.P. XI*)

*Average dose*—1 drachm. Contains about 20% of potassium citrate

**Sodii Citras** (*B.P., U.S.P. XI, P. Helv. V, P. Dan.*)

$\text{COONa} \cdot \text{C}(\text{OH})(\text{CH}_2 \text{COONa})_2 \cdot 2\text{H}_2\text{O} = 294.1$

*Dose*—15 to 60 grains (1 to 4 g.)

*Intravenously*, rabbits tolerate up to 0.4 to 1.6 g per kilo, suitably diluted, or approximately 6.4 to 25.6 g per 10-stone man (on Meeh's Formula, *qv*)

Granular crystals or powder. It is also obtainable with  $5\frac{1}{2}$   $\text{H}_2\text{O}$ , 6 of the latter = 5 of the official salt

**Soluble.** 1 in less than 2 of water, insoluble in alcohol 90%.

**Uses.** Used for the same purposes as the potassium salt. It has anticoagulant properties and is added for this reason to blood in transfusion. Solutions of strength 3.8% are used for washing out syringes and apparatus in blood transfusion and for mixing with the blood at the time it is drawn from the vein. 40 ml prevents coagulation of about 650 ml of blood. Although an anticoagulant *in vitro*, it accelerates coagulation when injected intravenously as a 5 to 30% *w/v* solution, or intramuscularly in doses of 15 ml of a 30% solution into each buttock. Intravenous injections should be made very slowly, using the finest possible needle.

Is used in feeding infants with cows' milk to prevent the formation of large clots, 1 gr per oz. being added. Up to 3 gr per oz. is sometimes used.

The citrate is thought to influence the clotting of milk by precipitating the bulk of the calcium salts. Some claim, however, that the citrate redissolves the precipitated salts.

**HÆMORRHAGE.** Intravenously prevents hæmorrhages at operations or delivery and from mucous membranes, e.g., epistaxis or metrorrhagia. Rise of vascular tension avoided by the following solution: Sodium citrate 20, magnesium chloride 10, water 100, inject 15 to 40 ml.—*J. Amer. med. Ass.*, 1/1926, 1170

**PNEUMONIA.** 30 to 40 grains every two hours may cause rapid lysis.



SEA-SICKNESS well treated by rectal injections of sodium citrate, 1 drachm to the pint, repeated according to retention and results. Also by the mouth from maximum dose of  $1\frac{1}{2}$  dr. every two or three hours, downwards—*Brit med J*, 1/1925, 140

THROMBOSIS (threatened or present)—Citrates given with good results—*E. Tylecote, Med. Pr.*, 1929, 261, H. F. Marriss, *Brit med J*, 11/1917, 822

**Tabellæ Sodii Citratis (B.P.C.)** contain 2 gr (0.12 g)

**Liquor Sodii Citratis Fortis (C.X.H.)**

Sodium citrate 1 gr, sterile water to 4 ml, which is sufficient to prevent the coagulation of 15 oz of human blood

**Wright's Solution.**

Sodium chloride 4, sodium citrate 1, water 120 For sinus washing—Pye's Surg. Handicraft.

**Bi-Citrol** (*Laboratoires Marimer, Paris, Wilcox, Jozeau, London*) Sodium dihydrogen citrate in granular powder. Dose—1 teaspoonful in half a glass of warm water, twice daily. Hepatic and biliary affections, hyperviscosity of the blood, and arthritic affections

[P1] **Citronin** (*Parke, Davis, London*)

Dose—1 or 2 drachms at intervals of not less than 3 or 4 hours. A preparation containing in each drachm sodium citrate  $2\frac{1}{2}$  gr, citric acid  $\frac{1}{2}$  gr, potassium guaiacolsulphonate 1 gr, Cascara Evacuant  $\frac{1}{2}$  m, fluid extract of ipecacuanha  $\frac{1}{2}$  m, ethylmorphine hydrochloride  $\frac{1}{2}$  gr. For treatment of bronchitis and cough following "colds"

## ACIDUM FORMICUM

B.P.C., P. Helv. V

H COOH = 46.02

Syn. AMINIC ACID

Dose—2 to 10 minims (0.12 to 0.6 ml) per os freely diluted, e.g., with mineral water. Hypodermically 2 to 15 minims of 1 in 1000 dilution of actual acid. It is better given as sodium salt.

A colourless liquid containing 24 to 26% w/w of H COOH, sp. gr. about 1.063. Miscible with water.

Note—Formic acid is obtainable also of sp. gr. 1.12 = 50%, 1.15 = 65%, 1.2 = 85%, 1.22 = 100% H COOH, as a rule the 25% acid is referred to. The stronger acids cause painful burns.

**Uses.** It is alleged that this acid (acting in a manner similar to cantharides) gives tone to the muscles and restrains muscular tremor, as in cases of paralysis agitans, and in chorea. It increases muscular energy and abolishes the sense of fatigue. It is employed, usually as one of the salts, in influenza, gout, rheumatism, tremors, etc.

Intramuscularly a very dilute solution is valuable in rheumatic affections. The injections are much less painful than if given subcutaneously and the pain is transient.

The acid was originally made from the red ant, *Formica rufa*. The stinging nettle, *Urtica dioica*, contains formic acid, and has long been employed as a tonic and diuretic.

Given intramuscularly, gave definite improvement after 6 or 7 injections in rheumatic affections. Sixty cases treated.—*Brit med. J. Fp1*, 1/1933, 100

**Estoform** (*Crookes Laboratories, London*). Orthoformic ester with extracts of wild cherry and senega in a glycerin-spirit base. Dose—From 2 to 4 teaspoonfuls 3 times daily diluted with water. An antispasmodic in bronchitis, coughs and asthma.

**Ephestoform** (*Crookes Laboratories, London*) Estoform with 1 gr per oz of ephedrine hydrochloride

**Bee Venom.**

Based on the suggestion that bee-keepers do not suffer from rheumatism, bee venom has been used therapeutically for various rheumatic affections. Preparations are available (*Allen and Hanburys, London, and Antibody Products, Watford*) in ampoules for intramuscular injection and in ointment form for local use.

Very satisfactory results with bee venom. The venom collected at the end of the summer is most potent—Frank Coke, *Brit med J*, 1/1934, 872

The following are further preparations—

**Apicosan** (*August Wolff, Bielefeld, Pharmaceutical Products, London*) Bee venom in physiological saline solution. Supplied in the following strengths—(1) "N" = 1 unit in 10,000 dilution, (2) I = 1 unit (ampoules of 1 ml contain 1 bee sting), (3) II = 3 units (ampoules of 1 ml contain 3 bee stings), (4) III = 9 units (ampoules of 1 ml contain 9 bee stings). It is given by intracutaneous injection, in gradually increasing dosage, in arthritis, gout, sciatica, lumbago, etc.

Used at the Royal Devonshire Hospital with excellent results in arthritis, fibrositis and neuritis—W Shipton and J B Burt, *Brit med J*, 1/1934, 778

**Forapin** (*Coates & Cooper, London*) Ointment of bee venom with salicylic acid and oil of mustard

**Sodii Formas** (*B.P.C.*)  $\text{H COONa}$ ,  $\text{H}_2\text{O} = 86.02$

*Dose*—5 to 20 grains (0.3 to 1.2 g) in solution, increased if desired to as much as 60 grains (4 g) *per diem*

A white alkaline powder soluble in water. A strong reducing agent and powerful antiseptic. *Incompatible with acids*

**Uses.** In cases of heart and kidney diseases it is stated to lessen the loss of albumin by the urine, although it has diuretic powers. Does not disagree with the stomach. Said to be non-toxic. Has been employed in phthisis and in pneumonia. Improves appetite, and mental and physical activity. Ocular fatigue has been treated with sodium formate instillation 1 in 50 to 1 in 30. Rheumatism has been improved by 15-grain doses.

Diphtheria has been treated with 5 to 10 minim doses of 25% solution in water every 4 hours.

**[P1] Elixir Formatum Compositum** (*B.P.C.*) *Syn* ELIXIR FORMATUM CUM STRYCHNINA

*Dose*—1 to 2 drachms (4 to 8 ml.)

Contains per drachm approximately 3 gr each of sodium and potassium formates and 1½ m of solution of strychnine hydrochloride, in simple elixir

**Calcii Formas.**  $(\text{H} \cdot \text{COO})_2\text{Ca} = 130.1$

*Dose*—3 to 10 grains (0.2 to 0.6 g)

White crystals soluble 1 in 8 of water. More permanent than the sodium salt. Has been found useful for hæmorrhages

**Ferri Formas** (*B.P.C.*) *Syn* FERRIC FORMATE

$\text{Fe}_2(\text{OH})_2(\text{HCOO})_4 \cdot 4\text{H}_2\text{O} = 588.7$

*Dose*—1 to 5 grains (0.06 to 0.3 g)

Copper crystals soluble 1 in 18 of water forming an unstable solution, and 1 in 20 of dehydrated alcohol

**Lithii Formas.**  $\text{H COOLi}$ ,  $\text{H}_2\text{O} = 69.96$  White crystalline powder freely soluble in water

*Dose*—1 to 5 grains (0.06 to 0.3 g) As much as 1½ g of this salt have been given daily

**Uses.** Similar to the sodium salt and has been given in gout

**Magnesiæ Formas.**  $(\text{H}\cdot\text{COO})_2\text{Mg}\cdot 2\text{H}_2\text{O} = 150\cdot 4$ .

*Dose* — 3 to 10 grains (0·2 to 0·6 g.).

Colourless deliquescent crystals soluble in water

**Potassii Formas (B.P.C.).**  $\text{H}\cdot\text{COOK} = 84\cdot 11$

*Dose* and use similar to the sodium salt.

Crystalline hygroscopic powder very soluble in water forming neutral solution

[P1-81 88] **Strychninæ Formas.**

$\text{C}_{21}\text{H}_{21}\text{O}_2\text{N}_2$ ,  $\text{H}\cdot\text{COOH} = 380\cdot 2$ .

*Dose.* —  $\frac{1}{64}$  grain (0·001 g.), by hypodermic injection.

White crystalline powder, soluble in water about 1 in 5. A nerve stimulant and muscular tonic.

[P1] **Acidum Oxalicum (B.P.C.).**  $(\text{COOH})_2\cdot 2\text{H}_2\text{O} = 126\cdot 0$ .

[P1] "*Oxalic acid, metallic oxalates other than potassium quadroxalate.*"

[P2] "*Potassium quadroxalate*"

White crystals soluble in water about 1 in 12; a powerful poison, made by acting on wood, sugar, starch, etc., with sodium hydroxide

The toxicity of this acid in dilute solution and of its salts is due to their forming an insoluble calcium salt, a sufficient quantity of calcium in solution being essential for the welfare of the organism. Strong solutions of the acid are poisonous by corrosive action. Toxic symptoms and cardiac depression can be relieved by giving soluble calcium salts

**Antidotes.** Give immediately 2 dr of chalk or magnesia mixed with water. Empty stomach, using cautiously a soft stomach tube with 4 oz. of magnesia in 2 gallons of water. Do *not* give hydroxides or carbonates of potassium, sodium or ammonium, as these form soluble oxalates. Give 1 oz of castor oil. Keep the patient warm. Saline infusion with dextrose for collapse.

Is used for removing ink stains, iron mould, cleaning leather, etc., and removing the colour from calico printing

[P2] **Potassii Quadroxalas (B.P.C.)** *Syn.* SAL ACETOSELLA, POTASSIUM TETROXALATE, SALT OF SORREL, SAL LIMONIS, SALTS OF LEMON.

$\text{KHC}_2\text{O}_4\cdot \text{H}_2\text{C}_2\text{O}_4\cdot 2\text{H}_2\text{O} = 254\cdot 1$

Colourless crystals soluble about 1 in 30 of water

[P1] **Potassii Binoxalas.** *Syn.* POTASSIUM ACID OXALATE  $\text{KHC}_2\text{O}_4\cdot 2\text{H}_2\text{O}$   
Formerly supplied as salts of lemon

[P1] **Potassii Oxalas,** the neutral salt,  $\text{K}_2\text{C}_2\text{O}_4$ , is added to blood as an anti-coagulant.

[P1] **Cerii Oxalas (B.P.C.).**

*Dose.* — 2 to 10 grains (0·12 to 0·6 g.), in powders or cachets.

A white or pinkish, granular, odourless and tasteless powder, obtained as a by-product in the separation of thorium from monazite, and consisting of about 50% of cerous oxalate,  $\text{Ce}_2(\text{C}_2\text{O}_4)_3\cdot 10\text{H}_2\text{O} = 724\cdot 4$ , with the oxalates of numerous other rare earths especially lanthanum, praseodymium and neodymium. **Insoluble** in water; soluble in dilute acids. Used in chronic

vomiting especially that of pregnancy, also in chronic diarrhœa, hysteria, epilepsy and migraine

[P1] **Cerocol** (*Coates & Cooper, London*) Colloidal cerium oxalate in tablets containing 0.05 g. In vomiting, especially of pregnancy

**Acidum Succinicum** (*B.P.C.*)  $(\text{CH}_2\text{COOH})_2 = 118.0$ .

*Dose*—5 to 10 grains (0.3 to 0.6 g.)

Obtained on destructive distillation of amber, or by fermentation of tartaric (dihydroxysuccinic) acid or malic acid, or as by-product in fermentation of sugar

Colourless crystals soluble 1 in 20 of water, 1 in 9 of alcohol.

**Asparagin.** *Syn* ALTHFEN, AMINOSUCCINIC ACID AMIDE

$\text{HOOC}(\text{NH}_2)\text{HC}(\text{CH}_3)\text{CONH}_2 \cdot \text{H}_2\text{O} = 150.1$  *Dose*—5 to 10 grains. White crystals, having a slightly acid reaction. May be obtained from *Asparagus officinalis*, and the roots of liquorice, belladonna, etc. Soluble 1 in 50 of water, also in acid and alkaline solutions. Insoluble in absolute alcohol and ether. An aqueous solution dissolves freshly precipitated mercuric oxide, and this has been used for hypodermic injection in syphilis. Has decided diuretic effect. For cardiac dropsy and chronic gout, 1 grain is given three times a day.

## ACIDUM GLYCEROPHOSPHORICUM

*B.P.C.*

$\text{C}_3\text{H}_5(\text{OH})_2\text{OPO}(\text{OH})_2 = 172.1$ .

*Syn* GLYCERYLPHOSPHORIC ACID, MONOGLYCERYLPHOSPHORIC ACID

*Dose*.—5 to 10 minims (0.3 to 0.6 ml.)

A dibasic acid prepared by heating glycerin with phosphoric acid *in vacuo*. Occurs as a colourless, odourless liquid containing the  $\alpha$  and  $\beta$  monoglycerides equivalent to about 20% *w/w* of  $\text{C}_3\text{H}_5\text{O}_4\text{P}$ . Sp. gr. 1.095 to 1.105. The chief constituent is the  $\alpha$  variety. The acid is readily decomposed into glycerin and phosphoric acid on heating.

Stronger solutions, namely, 25% (sp. gr. about 1.13) and 50% (sp. gr. about 1.30) are also obtainable.

**Uses of the Glycerophosphates.** Thought to aid metabolism, hence given in emaciation and generally for tonic action. The compound syrup and glycerin of glycerophosphates, the syrup of glycerophosphates with formates, and many of the milk and glycerophosphate preparations have tonic properties in debilitated conditions, *e.g.*, during convalescence from illness.

The glycerophosphates were originally introduced into medicine by Robin, on the grounds that lecithin (*qv*), an omnipresent, complex fatty body, contains its phosphorus in the form of the glycerophosphoric radical.

**Calcii Glycerophosphas** (*B.P.C., P. Dan., Fr. Ch., P. Belg. IV, P. Helv. V, P. G. VI, and P. Ital. V.*). *Syn.* NEUROSINA (*F.E. VIII*).  $\text{CaC}_3\text{H}_5(\text{OH})_2\text{PO}_4 \cdot 2\text{H}_2\text{O} = 246.2$ .

*Dose*.—3 to 10 grains (0.2 to 0.6 g.) or more *per os* in water, *vide infra*. *Hypodermically* 1 grain (0.06 g.) in 40 minims (2.5 ml.)

*Intravenously* 1 grain (0.06 g) in 100 minims (6 ml) is suggested by analogy with the lactophosphate.

A white crystalline powder consisting mainly of the  $\alpha$ -glycerophosphate. The  $\beta$ -glycerophosphate is less soluble, and usually contains added citric acid to increase the solubility. Calcium glycerophosphate is formed, together with choline, on the breaking up of lecithin in the process of digestion.

**Soluble** about 1 in 40 of cold water, but different makers' products vary according to whether the compound is mainly the  $\alpha$  or the  $\beta$  modification (The  $\alpha$  position is the terminal hydroxyl in glycerin and the  $\beta$  the central in combination with phosphoric acid) It is only slightly soluble in hot water, soluble also in glycerin, insoluble in alcohol.

**Incompatible** with mineral acids and with soluble carbonates and phosphates. Solutions decompose when heated.

### **Caseinum Glycerophosphaticum (B.P.C.)**

*Dose* —1 to 4 drachms (4 to 16 g)

Soluble casein with 2½% each of sodium and calcium glycerophosphates

**Glycolactophos** (Roberts, London), **Sanatogen** (Genatosan, Loughborough) and **Vitafer** (Southall Bros. & Barclay, Birmingham) are casein and glycerophosphate combinations used in neurasthenia, and enfeebled nervous conditions generally.

### **Ferri Glycerophosphas (B.P.C.)**

*Syn* FERRIC GLYCEROPHOSPHATE

*Dose* —1 to 5 grains (0.06 to 0.3 g) In yellow or greenish yellow scales containing 13 to 16% of Fe, together with alkali citrate. Slowly soluble in water.

### **Magnesii Glycerophosphas (B.P.C.)**

$\text{MgC}_2\text{H}_5(\text{OH})_2\text{PO}_4 \cdot 2\text{H}_2\text{O} = 230.4$

*Dose*.—5 to 10 grains (0.3 to 0.6 g.)

A white amorphous powder, soluble 1 in about 50 of water. May be rendered more soluble by addition of citric acid or alkali citrate.

1% of citric acid increases the solubility to about 1 in 35, 5% to 1 in 25, 10% to 1 in 20. Glycerophosphoric acid added gives the figures 1 in 33, 1 in 24, and 1 in 18 respectively.

### **Mangani Glycerophosphas. $\text{Mn C}_2\text{H}_5(\text{OH})_2\text{PO}_4 = 225.0$**

*Dose* —1 to 5 grains (0.06 to 0.3 g)

Pinkish amorphous powder, only slightly soluble in water.

The relative anæmia which is often associated with cardiac overstrain may well be treated by administering manganese glycerophosphate with hæmoglobin.

### **Potassii Glycerophosphas Liquidus (B.P.C.).**

*Dose* —10 to 30 grains (0.6 to 2 g.).

A colourless syrupy liquid containing about 50% w/w of the hydrated neutral potassium salts of  $\alpha$ - and  $\beta$ -glycerophosphoric acids, calculated as  $\text{C}_3\text{H}_7\text{O}_8 \cdot \text{PO}_3\text{K}_2 \cdot 3\text{H}_2\text{O} = 302.3$ . A 75% solution is also obtainable.

**Quininæ Glycerophosphas (B P C)** $(C_{20}H_{24}O_2N_2)_2, C_3H_5O_5P, 4H_2O = 892.6$ 

Dose — 1 to 10 grains (0.06 to 0.6 g)

Fr. Cx. has the compound with  $5H_2O$ , termed "basic" quinine glycerophosphate. White crystalline powder, soluble 1 in about 200 of water, and 1 in 40 of alcohol 90%.

**Sodii Glycerophosphas (B P C, P Ned V)** *Syn* SODIUM GLYCERYLPHOSPHATE.  $C_3H_7O_6PNa_2, 5\frac{1}{2}H_2O = 315.2$  *P Ital V, P Dan, P Belg IV, F E VIII* and *Fr Cx Supp 1926* have  $5H_2O$

Dose — 5 to 10 grains (0.3 to 0.6 g), *per os*, also given *hypodermically* in 3 to 5 grain doses

In crystalline masses or as a white powder, consisting of the  $\beta$ -glycerophosphate.

**Soluble** 1 in 4 of water.

**Sodii Glycerophosphas Liquidus (B P C)**

Dose — 10 to 30 grains (0.6 to 2 g)

A colourless or faintly yellow syrupy liquid consisting of a 50% *w/w* solution of the sodium salts of  $\alpha$ - and  $\beta$ -glycerophosphoric acids. A 75% *w/w* solution is also obtainable in commerce

**[P 81] Strychninæ Glycerophosphas.**Dose —  $\frac{1}{64}$  to  $\frac{1}{16}$  grain (0.001 to 0.003 g)

White crystalline powder, soluble in water

**[P 1] Metatone (Parke, Davis, London)** Glycerophosphates of strychnine ( $\frac{1}{350}$  gr per dr), calcium, potassium, sodium, manganese with vitamin B extract, etc. Dose — 1 to 2 drachms before and after meals. Tonic and restorative

**Emulsio Olei Morrhuæ cum Glycerophosphatibus (B.P.C)**Dose —  $\frac{1}{4}$  to 1 ounce (8 to 30 ml)

Contains 50% *v/v* of cod-liver oil with the glycerophosphates of calcium, magnesium, iron, sodium and potassium

**Jecovol (Woolley, Manchester)** is a proprietary emulsion of cod-liver oil with sodium, calcium and iron glycerophosphates

**Emulsio Paraffini Liquidi cum Glycerophosphatibus (B P C)** *Syn* EMULSIO PETROLEI CUM GLYCEROPHOSPHATIBUS

Dose — 1 to 4 drachms (4 to 16 ml.)

Contains 50% *v/v* of liquid paraffin with the glycerophosphates of calcium, magnesium, iron, sodium and potassium

**Extractum Malti Liquidum cum Glycerophosphatibus (B P C)**

Dose — 1 to 4 drachms (4 to 16 ml.)

Contains in 1 dr. the equivalent of  $\frac{1}{2}$  gr. each of potassium and sodium glycerophosphates, in liquid extract of malt

**Glycerinum Glycerophosphatum Compositum (B.P.C.)**  
*Syn.* ELIXIR GLYCEROPHOSPHATUM, GLYCEROL GLYCEROPHOSPHATIS

Dose — 1 to 2 drachms (4 to 8 ml)

Contains in 1 dr. calcium glycerophosphate  $1\frac{1}{2}$  gr, potassium,

sodium, and magnesium glycerophosphates of each about  $\frac{1}{2}$  gr., and iron glycerophosphate about  $\frac{1}{4}$  gr. It contains no sugar or strychnine

**Glycerinum Glycerophosphatum cum Medulla Rubra** (*B P C*). *Syn* GLYCEROL GLYCEROPHOSPHATIS CUM MEDULLA RUBRA, ELIXIR GLYCEROPHOSPHATUM CUM MEDULLA RUBRA

*Dose* —1 to 2 drachms (4 to 8 ml).

Equal parts of compound glycerin of glycerophosphates and extract of red bone marrow

**Granular Effervescent Glycerophosphates.**

*Dose* —60 grains (4 g.)

Contains in 1 dr., glycerophosphate of calcium 3 gr., of iron 1 gr., of magnesium 3 gr., of potassium 3 gr., with caffeine citrate 1 gr. A palatable mode of administration

[P1] **Syrupus Glycerophosphatum Compositus** (*B P C*)

*Syn* SYRUPUS GLYCEROPHOSPHATUM RUBER

*Dose* —1 to 2 drachms (4 to 8 ml).

Contains the glycerophosphates of calcium, sodium, potassium, magnesium and iron, with about  $\frac{1}{4}$  gr of strychnine and  $\frac{1}{2}$  gr of caffeine per drachm

**Syrupus Glycerophosphatum Compositus cum Medulla Rubra** (*B P C*.)

*Dose* —1 to 2 drachms (4 to 8 ml)

Equal parts of compound syrup of glycerophosphates and extract of red bone marrow

[P1] **Syrupus Glycerophosphatum cum Formatibus** (*B P C*)

*Syn*. COMPOUND ELIXIR OF GLYCEROPHOSPHATES WITH FORMATES

*Dose*.—1 to 2 drachms (4 to 8 ml.)

Contains the glycerophosphates of calcium, sodium, potassium, magnesium and iron, with about  $\frac{1}{4}$  gr of strychnine and 3 gr each of potassium and sodium formates per drachm.

[P1] **Syrupus Glycerophosphatum et Pepsini Compositus** (*B P C*.) *Syn* SYRUPUS GLYCEROPHOSPHATUM COMPOSITUS (Robin).

*Dose* —1 to 2 drachms (4 to 8 ml).

Contains the glycerophosphates of calcium, sodium, potassium, magnesium and iron, with about  $\frac{1}{2}$  gr of pepsin and 2 m of tincture of ignatia per drachm.

**Syrupus Glycerophosphatum Flavus** (*B P C*.)

*Dose*.—1 to 2 drachms (4 to 8 ml.)

It is of the same strength as *Syr. Glycerophosph. Co.*, but contains no strychnine, and is coloured yellow.

## ACIDUM HYDRIODICUM DILUTUM

(with METALLIC IODIDES)

*B.P.C., U.S.P. XI.*

*Dose*.—5 to 10 minims (0.3 to 0.6 ml) well diluted, or in syrup  
*U.S.P. average dose* 15 minims.

This acid is prepared by heating red phosphorus and iodine in presence of water, or by the action of hydrogen sulphide on a solution of iodine.

A colourless, odourless liquid containing 10% *w/w* of HI with 1% *w/w* of  $H_3PO_2$  added to prevent discolouration on keeping. Other strengths available in commerce are 20% with sp. gr. 1.17, 46 to 47% with sp. gr. 1.5, and the constant boiling acid containing 57% *w/w* and boiling at 125°

**Syrupus Acidi Hydriodici (B.P.C.).**

*Dose* —  $\frac{1}{4}$  to 1 drachm (2 to 4 ml.), well diluted

Dilute hydriodic acid 10% *v/v*, with distilled water and syrup

**Syrupus Acidi Hydriodici (U.S.P. XI)**

*Average dose* — 60 minims (4 ml.)

Diluted hydriodic acid (10%) 13 ml, sucrose 45 g, water to 100 ml.

**Glycerinum Acidi Hydriodici.**

*Dose.* — 20 to 60 minims in water, increased to 3 drachms.

Dilute hydriodic acid 1, glycerin  $4\frac{1}{2}$ , and water  $4\frac{1}{2}$ . Contains 1% hydriodic acid and has good keeping qualities

**Ammonii Iodidum (B.P.C., P. Helv. V)  $NH_4I=145.0$ .**

*Dose.* — 2 to 6 grains (0.12 to 0.4 g.).

White deliquescent crystalline granules becoming yellow on exposure to air, owing to loss of ammonia and liberation of iodine.

**Soluble** 1 in 1 of water, 1 in 3 of alcohol 90%, 3 in 4 of glycerin

It causes less depression than potassium iodide, and is preferred by some for syphilis and rheumatism

**ASTHMA (HUMID)** Ammonium iodide, tincture of sanguinaria, tincture of lobelia, of each 1 dr., syrup of tolu to 6 dr. One drachm in a little water every 2 to 4 hours — Bartholow.

**Calcii Iodidum (B.P.C.).  $CaI_2=293.9$ . Prop. Name CALCIDIN (Abbott, Montreal; Pharmaceutical Products, London), available in powder, tablets, or lozenges.**

*Dose* — 1 to 5 grains (0.06 to 0.3 g.). Given in dilute aqueous solution.

Deliquescent crystalline powder. On exposure to light or air will liberate iodine; best preserved in amber bottles. Excellent results in foul ulcers and chilblains.

**Elixir Calcii Iodidi.** *Dose* — 1 drachm (4 ml.) Calcium iodide 3 grains, aromatic elixir 1 drachm. Employed in tuberculosis.

[P1 81 84] **Calcidrine Syrup (Abbott, Montreal, Pharmaceutical Products, London).** Contains calcium iodide 7 gr., ephedrine hydrochloride  $\frac{1}{2}$  gr., codeine sulphate  $\frac{1}{2}$  gr., Nembutal  $\frac{1}{2}$  gr., syrup of wild cherry and syrup of tolu to 1 oz. Antispasmodic and sedative cough syrup

**Lithii Iodidum (B.P.C.).  $LiI=133.9$ .**

*Dose.* — 1 to 5 grains (0.06 to 0.3 g.)

White crystalline deliquescent powder becoming yellowish when stored. Contains theoretically 94.7% of I

**Soluble** in water and alcohol 90%.

An antiarthritic, and has been employed in syphilis, also in rheumatoid arthritis by iontophoresis.



**Umbrenal** (*Schering, London*) A 25% solution of lithium iodide in 12 ml ampoules Used as a contrast medium in pyelographic work

**Potassii Iodidum** (*B.P., U.S.P. XI, P. Dan.*)  $KI=166.0$

*Dose.*—5 to 30 grains (0.3 to 2 g.)—often much increased, even up to 4 drachms per day. *U.S.P. XI* average dose 5 grains; as antiluetic 30 grains

(**Kalium Jodatum** (*P.G. VI, P. Helv. V, Fr. Cx.*) is potassium iodide Potassium iodate,  $KIO_3$ , is called **Kalium Jodicum** in Germany.)

In white cubic crystals or granular powder **soluble** 1 in 0.7 of water, 1 in 12 of alcohol 90%, and 1 in 2 of glycerin.

Solutions become yellowish in colour on standing, especially when exposed to light, owing to the liberation of a trace of free iodine A slightly alkaline solution keeps better than an acid one

**Incompatible** in solution with Spiritus Ætheris Nitrosi (unless made alkaline), salts of iron (except Ferri et Ammonii Citras and Liquor Ferri Acetatis), salts of bismuth, lead and mercury, Liquor Strychninæ Hydrochloridi, quinine sulphate and other alkaloidal salts, and with silver nitrate and potassium chlorate

**Uses.** In universal use in the later stages of syphilis, in arteriosclerosis and in certain cases of gout and rheumatism. In rheumatoid arthritis may be given in conjunction with guaiacol carbonate Small doses are valuable in the early stages of bronchitis, rendering the secretion less viscid It also assists tuberculous expectoration Is useful in conjunction with creosote in lobar pneumonia (*vide* Mistura Creosoti et Potassii Iodidi)

For actinomycosis it is specific, very large doses are given Sporotrichosis and blastomycosis also respond. Acute parotitis is favourably treated with iodine externally and potassium iodide internally In tinnitus aurium associated especially with vertigo, due to labyrinthine disease, full doses may be given Is of value also in lymphangitis.

In aneurysm moderate to full doses are given The addition of ammonium bromide is often useful

In 5 to 15 grain doses twice or thrice daily, often with tincture of stramonium, is useful in asthma, both during the paroxysms and in the interval

In arteriosclerosis 3 to 5 grain doses thrice daily with potassium bicarbonate 5 to 10 grains, sal volatile 20 minims, and an ounce of gentian infusion continued for four months at a time with interruptions of 10 or 12 days One or two tablets of nitroglycerin as well to promote vascular relaxation—Yeo

In fibrositis it is perhaps the most valuable drug It appears to act by removing the hyperplasia and serous exudation in the fibrous tissues.

In areas where goitre is endemic, potassium iodide is administered prophylactically, but care must be taken to avoid overdosage and consequent hyperthyroidism. For this purpose it may be taken as *iodised table salt* containing about 1 in 200,000 of potassium or sodium iodide.

**IODINE THERAPY** Iodides may prevent or retard arterial changes and arrest them. Iodine metabolism no doubt responsible. The duration of life may be extended in the future.—W. Mitchell Stevens, *Lancet*, 1/1930, 1235

**CARDIO-VASCULAR SYPHILIS** Potassium iodide the most efficacious treatment, though explanation of its action is difficult. Iodine by injunction may be substituted. Mercury is not more effective than arsenic, but safer. 0.3 g of neoarsphenamine at intervals of a week over long periods, till 5 g have been taken. Iodide and mercury continuous, and a course of organic arsenic added from time to time.—Carey F. Coombs, *Brit med J*, 11/1930, 893

**GOITRE**—The Swiss Goitre Commission (1922) after exhaustive investigations fixed the maximum amount as 1 part iodine in 200,000 parts of salt. This is the amount adopted in this country. Marne in the U.S.A. advises 1 in 500 in mildly goitrous districts.—J. A. Goodfellow, *Brit med J*, 1/1925, 331

The amounts of iodine recommended by the Swiss Commission are too small for goitrous districts. Five to 10 mg of iodine weekly is sufficient for prevention among school children, and 10 mg per week should be given during pregnancy and lactation.—*Medicine*, 1924, 3, 453, per *Pharm J*, 1/1925, 546

Sweets containing  $\frac{1}{2}$  gr of iodine given every 5 days are a good preventive measure for children, and in many cases sufficient to effect a cure. The aim should be to ensure that the thyroid receives its normal iodine requirement, which is about 2 gr per year. Most cases of nocturnal incontinence also cured by the use of these sweets.—K. Fraser, Cumberland, School M.O. Report, 1925

From a trial in several Derbyshire schools iodised sweets not recommended.—P. H. J. Turton, *Lancet*, 11/1927, 1170

Hyperthyroidism resulting from use of iodine in goitres of long standing. Dosage should be considered in terms of milligrammes rather than of grains, the maximum dosage for an adult being 10 mg daily for not longer than one month, the patient being kept under very close observation during this time.—O. P. Kimball, *J. Amer med Ass*, 11/1925, 1710

It is not clear that all endemic goitres are of the same order, or due to the same cause, and no agreement as to the amount of iodine required to prevent simple goitre has been reached. The goitre problem seems to be a domestic one for each locality.—*Brit med J*, 1/1925, 321

Iodine stimulates intestinal movements and in excessive doses causes diarrhoea. By the mouth potassium iodide causes a rapid rise in the iodine content of the blood. It is only in exceedingly high dosage that iodine causes injury to the sex glands—no injurious effects occur with small or moderate dosage. In the human subject the minimum amount of iodine required daily for an adult male is calculated at 15 microgrammes (millionths of a gramme). The dosage necessary to prevent goitre is higher, and the lower physiological limit is placed at about 100 microgrammes per day.—*Spec Rep Ser med Res Coun*, Lond, No 123, 1929

**L.IPROSY** Extremely useful in the last stages of recovery, but should only be used in patients maintaining a high resistance and tolerating full doses of Hydnocarpus esters.—E. Mur, *Trans R Soc trop Med Hyg*, Aug, 1931, 94

**Toxic Effects.** Idiosyncrasy to iodides sometimes occurs, comparatively small doses producing nasal catarrh, lachrymation, skin rashes and headache

### **Linimentum Potassii Iodidi (B.P.C.)**

A fluid liniment containing potassium iodide 1 in 10

### **Linimentum Potassii Iodidi cum Sapone (B.P.C.)**

A solid liniment containing potassium iodide about 1 in 7 with curd soap, glycerin, oil of lemon and water

**Absorption.** Potassium iodide solution, even with soap present, is not absorbed by the skin, but when applied as an emulsion in such substances as soft paraffin, lanolin and stearic acid, it can be detected in the urine within 12 hours.—*J. chem Soc Abstr*, 1/1925, 1116

### **Mist. Pot. Iod. (N.F.)**

Potassium iodide  $2\frac{1}{2}$  gr., ammonium carbonate  $2\frac{1}{2}$  gr., concentrated compound infusion of gentian 15 m, chloroform water to  $\frac{1}{2}$  oz

**Pilula Potassii Iodidi.** Contains 1 grain or more Potassium iodide 1 gr., exsiccated sodium carbonate  $\frac{1}{2}$  gr., with tragacanth and syrup Tablets and capsules contain 5 grains.

**Potion Iodurée.**

Potassium iodide 0.5 g., syrup of orange 25 g., distilled water 100 ml., to be taken in three portions during the day.

**Unguentum Potassii Iodidi (B.P.C.).**

10% with potassium carbonate in water and benzoinated lard.

[P1] **Mixed Treatment Tablets** (*Parke, Davis, London*). Potassium iodide, syrup of ferrous iodide, mercuric chloride  $\frac{1}{2}$  gr., solution of arsenous and mercuric iodides 2 m., tincture of nux vomica 4 m

Dose—1 to 3 tablets Syphilis, tabes, etc.

**Sodii Iodidum (B.P., U.S.P. XI, P. Dan.).** NaI = 149.92.

Dose.—5 to 30 grains (0.3 to 2 g.). U.S.P. XI average dose 5 grains

(**Natrium Jodatum**, *P. Helv V, P.G., Fr. Cx.*, is sodium iodide. Sodium iodate is called **Natrium Jodicum** in Germany.)

A white crystalline deliquescent powder, **soluble** 3 in 2 of water and 1 in 3 of alcohol 90%. Must be crystallised at a temperature above 20° otherwise the hydrated salt with 2H<sub>2</sub>O is obtained.

**Uses** and incompatibility similar to those of the potassium salt, *q v*

GOITRE is endemic in the valleys of E and N.E Lancashire. 2½ or 3 grains of sodium iodide thrice daily for six weeks, then discontinued for a month and resumed indefinitely Large goitres disappear—R. Stewart, *Brit med. J.*, 11/1921, 843

Small doses of iodide, *e g*, sodium iodide 3 gr. daily, for 10 days each spring and autumn found efficacious in girls in reducing the number of cases of goitre in districts where it is endemic, and it is not unreasonable to expect that by reducing the tendency to *simple goitre in early life*, we may also lessen the number of cases of *Graves' disease occurring in later life* This preventive treatment is, however, quite *unsuited for those who already show signs of hyperthyroidism*.—G R Murray, *Brit med J.*, 11/1922, 908

GOITRE well treated by six intravenous injections on alternate days of 6 gr. in 5 ml water—Reddi, *Prescriber*, 1928, 159.

HERPES ZOSTER Intravenous injection of sodium iodide 20 ml of 10% solution on the 1st, 2nd, 4th and 7th days (some patients less). also a dusting powder of zinc oxide, camphor, starch and morphine. All cases cleared up in less than 17 days.—*Prescriber*, 1931, 352

PARESIS Usual dose—1 g in 10 ml of water. Doses of 100 ml of 10% solution generally well tolerated at 4 to 7-day intervals Give preliminary test dose of 20 ml As much as 30 to 50 g has been injected in one dose.—*J Amer. med Ass*, 11/1929, 1753

SYPHILIS OF THE CENTRAL NERVOUS SYSTEM Injection of sodium iodide solution 10%, from 10 to 100 ml, seemed to have beneficial effects. The dissolving of Salvarsan substitutes in sodium iodide solution is suggested.—*J. Pharmacol*, June, 1926, 355.

[P1 81] **Mistura Sodii Iodidi Composita.**

Dose.—1 drachm (4 ml) thrice daily for an adult.

Sodium iodide  $\frac{1}{2}$  dr., sodium benzoate 3 dr., arsenical solution  $\frac{1}{2}$  dr., tincture of pulsatilla 1 dr., tincture of baptisia 3 dr., syrup of orange 1 oz., chloroform water to 8 oz.

In tuberculosis this mixture is of service. Calcium salts in large quantities also essential.

**Sodium Iodide as Pyelographic Medium.**

*U C H.* has a sterile solution of sodium iodide 15 g. in distilled water to 50 ml.

**PYELOGRAPHY** 13.5% sodium iodide is best. Renal function and pyelography are mutually interdependent—*Lancet*, 1/1929, 1160

Prolonged anuria in a woman following injection of sodium iodide 15% into pelvis for pyelography. Relieved by venesection—D. D. Pinnock and I. W. Matthews—*Lancet*, 11/1931, 529.

**Strontii Iodidum** (*B P C.*).  $\text{SrI}_2 \cdot 6\text{H}_2\text{O} = 449.6$ .

*Dose.*—5 to 15 grains (0.3 to 1 g.).

In deliquescent crystalline masses, with bitter saline taste.

**Soluble** 2 in 1 of water, and in alcohol.

Exophthalmic goitre of children has been treated with this and the bromide, also asthma, rheumatism, and chronic endocarditis

**Zinci Iodidum** (*B P C.*).  $\text{ZnI}_2 = 319.2$ .

*Dose*— $\frac{1}{2}$  to 2 grains (0.03 to 0.12 g.)

A white deliquescent powder turning brown on exposure. For cerebral, spinal, and nervous diseases in the third stage of syphilis, and in epilepsy, but rarely used

**Talbot's Solution** (*Can Form*) Zinc iodide 110 gr., distilled water 82 m, iodine 183 gr., glycerin to 1 oz

**Acidum Iodicum**  $\text{HIO}_2 = 175.9$ .

*Dose*—1 to 5 grains (0.06 to 0.3 g.)

White crystalline powder very soluble in water. It is employed in ozæna, for deodorising offensive urine, as an irrigant in empyema (strength 1 in 500) and for leg ulcers, as a mouth-wash, e.g., in inoperable epithelioma, and as a throat swabbing in diphtheria. Internally a drachm of a 1 in 100 solution, well diluted, has been given in gastro-intestinal sepsis, as in typhoid fever. The calcium salt is principally employed.

**Calcii Iodas.**  $\text{Ca}(\text{IO}_3)_2 \cdot 6\text{H}_2\text{O} = 498.0$  *Syn* CALCINOL.

*Dose*—3 to 4 grains 3 times daily in solution

Tasteless, odourless powder, soluble in 380 parts of water at 11.5°. Acts equally well in an acid or alkaline medium as a deodorant and anti-putrefactive.

**Lotio Calcii Iodatis** (saturated aqueous solution) is employed in septic and suppurating wounds. A warm saturated solution is used as a vaginal douche or bladder irrigant, efficient as a mouth-wash or gargle.

**Sodii Iodas.**  $\text{NaIO}_3 = 197.9$  1½ grains in 5% solution (about saturated) has been injected for acute and chronic articular rheumatism

**ACIDUM HYDROBROMICUM**

(with METALLIC BROMIDES)

*B P C.*

$\text{HBr} = 80.92$ .

Hydrobromic acid of sp. gr. 1.303 to 1.314 and containing about 34.5% w/w of HBr. Liquid with an acrid smell. Should not be exposed to sunlight. It may be prepared by the action of bromine on amorphous phosphorus in the presence of water and is colourless or straw-coloured. Commercially the acid is also

obtainable in the following strengths—25% *w/w* (sp gr. 1.208), 30% *w/w* (sp gr. 1.260), and 40% *w/w* (sp gr. 1.375) *P Ned* is 4N (about 32%)

**Acidum Hydrobromicum Dilutum** (*B P*, *Fr Cx*, *P Helv. V*)

*Dose*.—15 to 60 minims (1 to 4 ml), 60 minims = 10 grains of potassium bromide approximately. Contains 10% *w/w* of *HBr*. Sp gr 1.072 to 1.075. An acid of approximately the same strength is obtained by diluting 290 g of the concentrated acid with 710 g of water (approximately 4 fl oz 6 fl dr to 20 fl oz)

*Uses*. To allay nervous excitability and exhaustion, and as an alternative to potassium bromide, given with morphine to allay after-effects. As a solvent for quinine and to prevent quinism 8 minims will dissolve 5 grains of quinine sulphate in water. Obviates the sense of fulness of the head felt when taking iron. It is useful for tinnitus aurium and tickling hacking cough in doses of 10 minims, and in headache, with flushing of the face and ringing in the ears. In vertigo it is successful and it relieves toothache. In epilepsy, up to  $\frac{1}{2}$  ounce well diluted may be given, even to 3 ounces daily.

[P] **Mistura Chloroformi Composita** (*B P C*) *Syn* MISTURA TUSSI SEDATIVA, MISTURA TUSSI RUBRA

*Dose* — $\frac{1}{2}$  to 1 drachm (2 to 4 ml)

Contains 15 m of dilute hydrobromic acid and  $\frac{1}{10}$  gr of morphine hydrochloride per drachm

**Ammonii Bromidum** (*B P C*, *U S P XI*, *P Helv. V*, *P Dan.*).  $\text{NH}_4\text{Br}$  = 97.96

*Dose* —5 to 30 grains (0.3 to 2 g.)

Small colourless crystals. **Soluble** 2 in 3 of water, 1 in 13 of alcohol 90%. **Incompatible** with mineral acids, silver nitrate and spirit of nitrous ether

*Uses*. Possesses similar sedative properties to those of the other bromides (*vide* Potassii Bromidum) and is thought to cause less depression

In sea sickness ammonium bromide, beginning a day or so before the voyage, in doses of 20 gr in chloroform water with 15 gr of sodium bicarbonate thrice a day, has been found useful

In tinnitus a course of ammonium bromide with compound syrup of glycerophosphates does well. The bromide at bedtime — Sir James Barr

**Pastilli Ammonii Bromidi** (*B P C*) contain 1 gr (0.06 g.)

**Tabellæ Ammonii Bromidi** (*B P C*) contain 5 gr (0.3 g.)

**Ammonii Bromidum Effervescens** (*B P C*).

*Dose* —75 grains to 1 ounce (5 to 30 g.). 1 in 12 $\frac{1}{2}$

**Mistura Ammonii Bromidi, Phenazoni et Caffeinæ.**

*Dose* —1 ounce (30 ml.), repeated in two hours if necessary

Ammonium bromide 10 gr., phenazone 10 gr., caffeine citrate 5 gr., chloroform water to 1 oz

Ordinary headache is rapidly relieved by this.

**Calcii Bromidum** (*B P C*, *U S P XI*, *P Helv V*, *P. Dan*)  
 $\text{CaBr}_2 \cdot 2\text{H}_2\text{O} = 235.94$

*Dose* —8 to 30 grains (0.5 to 2 g.)

A very deliquescent white crystalline powder with saline, bitter taste

**Soluble** 1 in 0.3 of water and 1 in 0.6 of alcohol 10%

When the aqueous solution is recrystallised the salt  $\text{CaBr}_2 \cdot 6\text{H}_2\text{O}$  is obtained. It is converted into  $\text{CaBr}_2 \cdot 2\text{H}_2\text{O}$  by heating to  $180^\circ$

*Fr Cx Supp* 1926 allows 20 to 25% of water. This salt is obtained by solidification of the molten mass in its water of crystallisation

**Uses.** Is effective in epilepsy and sometimes preferred to potassium bromide. Has been given intravenously in asthma, hay fever and anaphylactic shock, and for preventing post-operative bleeding in obstructive jaundice

**Calcibronat** (*Sandoz, London*) Calcium brom-lactobionate. Issued in granules and effervescent tablets. Indications as for bromide therapy

**Lithii Bromidum** (*B P C*)  $\text{LiBr}$  86.86

*Dose* —5 to 15 grains (0.3 to 1 g.)

White, deliquescent, slightly bitter granules, with neutral reaction. Contains a variable amount of moisture, but less than one molecule

**Soluble** 5 in 3 of water, readily soluble in alcohol 90%

Contains 91% of bromine as against 67% in potassium bromide, hence effect is greater, especially as a hypnotic, and in epilepsy

**Magnesi Bromidum** (*B P C*)  $\text{MgBr}_2 \cdot 6\text{H}_2\text{O} = 292.2$

*Dose* —5 to 20 grains (0.3 to 1.2 g.)

Contains 54.9% of bromine. Given in hysteria and epilepsv as a nervine sedative. Soluble 1 in 0.6 of water and 1 in 2 of alcohol 90%

**Mangani Bromidum.**  $\text{MnBr}_2 \cdot 4\text{H}_2\text{O}$  286.8

*Dose* —1 to 3 grains (0.06 to 0.2 g.)

Contains 55.7% of bromine, and is given as a nervine tonic. It is soluble 1 in less than 1 of water and alcohol

**Potassii Bromidum** (*B P*, *U S P XI*, *P. Dan*)  $\text{KBr} = 119.0$

*Dose* —5 to 30 grains (0.3 to 2 g.) *U S P XI* average dose 15 grains

Small doses, e.g. 5 grains once a day long continued, are better in functional nervous disorders than larger doses for shorter periods—M. Craig, *Lancet*, 11 1917, 979

**(Kalium Bromatum** (*P G*, *P Helv V*, *Fr Cx*, *P Hung*) is potassium bromide. Potassium bromate,  $\text{KBrO}_3$ , is called **Kalium Bromicum** in Germany)

Colourless or white crystals with saline taste. **Soluble** 1 in about 2 of water, and 1 in about 200 of alcohol 90%

**Incompatible** with mineral acids, mercury and silver salts

**Toxic Effects.** Prolonged administration may cause symptoms of bromism, including nausea, dullness and muscular weakness with acneiform or erythematous rashes. To avoid the onset give arsenical solution together with purgatives and salol. Patients saturated with bromides exhibit anæsthesia of the palate—a little known but useful diagnostic. Tickling the palate with a

feather is a good means of eliciting the information. The effect of bromides is enhanced by adding potassium bicarbonate in doses equal to about a quarter of the total bromide given

Bromide intoxication has been treated with 100 ml of normal saline increased to 400 ml intravenously

**BROMISM** The early symptoms of bromide intoxication are an exaggeration of the therapeutic sedative effect. Definite retardation of thought, speech, and action appears, with anorexia, constipation, weakness and drowsiness. This stage is seldom dangerous if recognised before the appearance of frank psychosis, and the symptoms clear up gradually when the bromide is discontinued. If the drug continues to accumulate, outspoken psychosis frequently occurs. Drowsiness and lethargy may be replaced by insomnia and irritable restlessness. The patient refuses food and fluids, and may become severely dehydrated. Dry mucous membranes, furred tongue, foul breath, dilated pupils, ataxia and tremulousness are typical symptoms of the more severe states. Symptomatic or delirious psychotic manifestations appear. In some cases, skin lesions appear, but the skin may be normal in the presence of outspoken mental disturbance. Dependence upon the bromide crupion as a diagnostic aid is one of the chief reasons why symptomatic psychoses due to bromide pass unrecognised. A blood bromide level of 250 mg per cent or higher will account for a delirious psychosis in a patient who is in fairly good physical condition.—P. W. Preu, J. Romano and W. T. Brown, *New Engl J Med*, 1936, 21, 57

**Uses.** Hypnotic and sedative. Much used in epilepsy, greatly reducing the number of fits. In recent epilepsy should be given for a long period (not less than two years). If no benefit from 45 to 75 grains per diem some other remedy should be tried. (It is cumulative.) Addition of belladonna may be useful where there is incontinence.

The following mixture has been recommended—

Potassium bromide 1 oz, potassium iodide 2 dr, ammonium bromide 3 dr., ammonium carbonate 1 dr, tincture of calumba 1 oz., water to 6 oz. One teaspoonful before each meal and three teaspoonfuls at bedtime. If *petit mal* exists alone, or co-exists with complete epilepsy, the dose of ammonium bromide must be increased and that of the other diminished.

Valuable especially in combination with chloral hydrate, in insomnia due to worry or overwork but not to pain. Large doses have been given in tetanus, and it has also been used as an antidote to strychnine poisoning. Sedative in spermatorrhœa and nymphomania. For gonorrhœal erections 15 to 35 gr may be given 2 to 4 times daily in a cachet with lupulin 1 to 2 gr and camphor 1 to 2 gr. In combination with belladonna it has been used in puerperal eclampsia.

Bromide must not be administered over any prolonged period unless an adequate intake of fluids and chloride is maintained, and the physician should be constantly alert for symptoms of bromide intoxication. Bromide should not be employed in states of severe excitement and agitation because it is not effective unless dangerously large doses are given. Bromide should never be used in cases of delirium due to either toxic or infectious causes. It should be used with caution in cases of arteriosclerosis, since delirium is readily produced if cerebral arteriosclerosis is present. Nephritis is a definite contraindication to the use of the drug. Bromide should not be used in cases of dehydration or severe malnutrition, in which the body fluids and chlorides are low.—P. W. Preu, Romano J, and W. T. Brown, *New Engl Med J*, 1936, 214, 61

**LABOUR.** A combination of potassium bromide and chloral hydrate is a safe and useful sedative in the first stage of labour, especially in excitable and nervous patients, and does not appear to lessen uterine contractions. Initial

dose, 30 gr. of each drug, repeated in smaller doses at 3 or 4-hourly intervals. Vomiting avoided by sipping the mixture dissolved in at least 6 ounces of water with glucose and lemon juice—L. McIlroy and H. Rodway, *J. Obstet. Gynec.*, 1933, 1175.

**LOCAL ANÆSTHETIC.** Forty-five operations, including two gastro-enterostomies and two lip cancer operations, done under local anæsthesia from injection of a 1% solution of potassium bromide—*J. Amer. med. Ass.*, 11/1925, 235

### Enema Potassii Bromidi (B.P.C.).

*Dose*—5 ounces (150 ml).

Potassium bromide 1% *w/v*, acetylsalicylic acid 0.5% *w/v* and mucilage of tragacanth in normal saline

### [P1] Mistura Bromidi Composita (B.P.C.).

*Dose*.— $\frac{1}{2}$  to 1 ounce (15 to 30 ml).

1 oz. contains 10 gr. each of the bromides of ammonium, potassium and sodium, and 10 m. of tincture of nux vomica.

### [P1] Mist. Pot. Brom. c. Strych. (N.I.F.)

Potassium bromide 10 gr., solution of strychnine hydrochloride 3 m., solution of bordeaux B 2  $\frac{1}{2}$  m., chloroform water to  $\frac{1}{2}$  oz

### [P1] Mistura Bromidi et Digitalis (St. M. H.)

Potassium bromide 20 gr., tincture of digitalis 5 m., potassium citrate 15 gr., compound tincture of cardamom  $\frac{1}{2}$  dr., peppermint water to 1 oz

### [P1] Mist. Bromidorum (N.I.F.)

Borax 5 gr., potassium bromide 5 gr., sodium bromide 5 gr., ammonium bromide 5 gr., arsenical solution 1 m., liquid extract of liquorice 5 m., chloroform water to  $\frac{1}{2}$  oz

### [P1] Mistura Dysmenorrhœica (E.G.A.)

Potassium bromide 15 gr., sal volatile, tincture of hyoscyamus *a.a.*  $\frac{1}{2}$  dr., spirit of chloroform 10 m., water to  $\frac{1}{2}$  oz.

**Tabellæ Potassii Bromidi (B.P.C.)** contain 5 gr. (0.3 g.)

[P1 31 34] **Brom-Nervacit** (*Brom-Nervacit, London*) Potassium bromide 4, sodium phosphate 0.1, diethylbarbituric acid 0.33, phenyldimethylpyrazolone 0.67, alcohol 7.5, saccharin 0.02, caramel 0.02, tincture of orange 0.1, tincture of cinchona 0.1, distilled water to 100. In hysteria, neurasthenia, etc.

**Cerebrom** (*C.F. Thackray, Leeds*) A flavoured bromide preparation. Each fluid drachm contains potassium and sodium bromide 5 gr., ammonium bromide 3 gr., calcium bromide 1  $\frac{1}{2}$  gr., lithium bromide  $\frac{1}{2}$  gr. *Dose*—1 to 2 fluid drachms diluted

**Sedin** (*Hommel's Hæmatogen Co, London*) Tablets contain potassium bromide and sodium bromide of each 0.4 g., ammonium bromide 0.2 g., with vegetable extractive. To make a sedative bouillon

[P1 31] **Gelineau Dragées** (*Mousmier-Delorme, Antony (Seine), Wilcox, Jozeau, London*) Dragées contain potassium bromide 1.0 g., antimony arsenate 0.001 g., picROTOXIN 0.0005 g. *Dose*—1st week, 1 twice daily, 2nd and 3rd weeks, 1 thrice daily, 4th week, 1 four times daily, and this dose (or larger if necessary) continued for 6 months or longer. For epilepsy. [P1] **Gelineau Sedative Syrup** contains in each fluid ounce 30 gr. of potassium bromide, 20 gr. of chloral hydrate and 3 m. of Fowler's solution. For insomnia.

**Sodii Bromidum (B.P., U.S.P. XI, P. Dan.).** Na Br = 102.9

*Dose*.—5 to 30 grains (0.3 to 2 g.). *U.S.P. XI* average dose 15 grains.

**(Natrium Bromatum (P.G., P. Helv. V, Fr. Cx., P. Hung.)** is sodium bromide. Sodium bromate, NaBrO<sub>3</sub>, is called **Natrium Bromicum** in Germany.)

In white deliquescent granular crystals, with saline taste.

**Soluble** 1 in 1  $\frac{1}{2}$  of water, 1 in 16 of alcohol 90%.

**Uses.** In insomnia, maniacal attacks and hysteria. Full doses



combat morphine habit, and may be given as a sedative in alcoholism. A 1% solution has been given by subdural injection, after removal of 50 to 60 ml of cerebrospinal fluid, for delirium tremens

A mixture of bromides in the proportion of sodium bromide 2, potassium bromide 2, and ammonium bromide 1, is said to have a better action than one salt alone

It is used as a substitute for salt in the "saltless" ("hypochloridisation") treatment of epilepsy (*See also Sodium Phosphate*.) The theory is that diminishing the chloride increases the readiness with which bromide enters the blood stream and nerve elements, *cf* Dechlorination, p 59

10 ml. of 10% solution intravenously has been recommended in eczema. 2 to 5 injections usually sufficient but more are sometimes needed

The addition of 20 drops of sal volatile, or 5 drops of Fowler's Solution to each dose prevents the rash which often disfigures patients taking bromide

**EPILEPSY**—The following is a typical hospital mixture for treatment of epilepsy sodium bromide 5 to 15 gr, borax 5 to 10 gr, tincture of belladonna 5 to 10 m, liquor arsenicalis 1 to 3 m, chloroform water to  $\frac{1}{2}$  oz Dose — $\frac{1}{2}$  ounce thrice daily after meals —D Brinton, *Practitioner*, 1/1936, 521

**HYPERCHLORHYDRIA**—Sodium bromide, 2 to 3 g a day Harmless in doses of 6 to 7 g even when continued for some time —*Brit med J Epit*, 1/1936, 60

**TABES**—Intrathecal injection of 1% sodium bromide tried In spastic patients, 1 6% (isotonic with body fluids) 10 ml of cerebrospinal fluid removed and the same quantity of solution introduced —*Lancet*, 1/1923, 607

**TRIGEMINAL NEURALGIA**—Many patients find considerable temporary relief, at least in the earliest stages, from the following mixture sodium bromide 10 gr, tincture of gelsemium 10 m, butylchloral hydrate 5 gr, peppermint water to  $\frac{1}{2}$  oz Dose — $\frac{1}{2}$  ounce thrice daily, after meals —D Brinton, *Practitioner* 1/1936, 526

**RADIOGRAPHY**—*Gall-bladder and gall-stone pictures* have been obtained following administration by the mouth of a single dose of 10 to 20 g of sodium bromide or strontium bromide dissolved in 100 or 150 ml of water. Rontgenograms taken 5 to 12 hours afterwards Patient should be on very light diet the preceding day

A 25% solution, introduced through ureteric catheters, has been used in pyelography

Ammonium bromide preferable to the sodium salt in pyelography, a 25% aqueous or glycerin solution being used —*Brit med J Epit*, 11/1927, 105

**Brosedan** (*Temmler, Berlin, Coates & Cooper, London*) A sodium bromide and vegetable yeast extract preparation One teaspoonful = 15 gr of NaBr.

**Sebrex** (*Allen & Hanburys, London*) Sedative broth tablets containing 17 grains of sodium bromide

**Sedobrol Tablets** (*Hoffmann-La Roche, London*) weigh 2 g, and contain 1 1 to 1 2 g of sodium bromide and 0 1 g of sodium chloride, in addition to vegetable extractives and fat Suggested for salt-free bromide treatment or diet—the tablet being simply covered with 100 to 200 ml of hot water to produce a bouillon for use in nervous affections, epilepsy and migraine

Dose—1 to 6 tablets *per diem*.

**Strontii Bromidum (B.P.C)**  $\text{SrBr}_2 \cdot 6\text{H}_2\text{O} = 355\cdot6$ .

Dose.—5 to 30 grains (0·3 to 2 g.).

In deliquescent crystals, with bitter saline taste, **soluble** 2 in 1 of water, 1 in 3 of alcohol

**Used** in gastric affections, dyspepsia, and vomiting of nervous origin; also in epilepsy instead of the potassium salt, but is more slowly absorbed

**Ekzebrol** (Tosse, Hamburg, Pharmaceutical Products, London) 10% strontium bromide solution *Dose*—10 ml intravenously daily for 3 or 4 injections in acute cases or 6 to 10 in chronic cases Eczema and other skin diseases

## ACIDUM HYDROCHLORICUM

(with METALLIC CHLORIDES)

HCl = 36.46

[P2] "*Hydrochloric acid*"

[83] "*Hydrochloric acid—in substances containing less than 9%, weight in weight, of hydrochloric acid (HCl)*"

*B.P.* has sp. gr. 1.158 to 1.168, containing 32% w/w of HCl *P. Ned. V* and *P. Helv. V* 25% *Fr. Cx* and *F.E. VIII* 33.65% *P.G. VI* 24.8 to 25.2% *P. Ital. V* 35.39% *P. Belg. IV* 36.47% *U.S.P. XI* 35 to 37%

**Incompatible** with alkalis, alkaline carbonates, metallic oxides, silver and lead salts

**Antidotes.** Treat as for poisoning by glacial acetic acid, see p. 7

**Use.** Escharotic Neuritis is sometimes treated by applying strong hydrochloric acid to the skin along the line of the inflamed and painful nerve on a wad of cotton wool, results are striking and appreciated (H. Wingfield's treatment)

The freshly diluted acid, 5 to 10 m with 6 to 8 oz. of water (Bouchard's remedy), taken with every meal, is of value in alimentary toxæmia

### Acidum Hydrochloricum Dilutum (*B.P.*)

*Dose.*—5 to 60 minims (0.3 to 4 ml.)

Is prepared by diluting 31.3 g. of the strong acid with water to 100 g. An acid of approximately the same strength is obtained by diluting 5 fl. oz. 310 m. of the strong acid with water to 1 pint Sp. gr. 1.045 to 1.052 Contains (*B.P.*, *U.S.P. XI*, *P. Helv. V*, *F.E. VIII* and *F. Norsk*) 10% w/w of HCl *P. Ital. V* 8.07%, *P. Ned. V* is 4×N (14.5%), *P.G. VI* 12.4 to 12.6%, *P. Belg. IV* 7.29%, *P. Dan.* 7.05%.

**Use.** Tonic biliary stimulant In dyspepsia, where insufficiency of acid, and in achlorhydria associated with pernicious anæmia up to 2 dr. well diluted is taken with meals  $\frac{1}{2}$  to 1 dr. with meals has been recommended for tuberculous diarrhœa Gargle 1 in 50 to 1 in 100 for sore throat. When diluted forms a useful refrigerant drink and lotion

In dilatation of the stomach 10 to 15 minims after each meal may be given with or without 6 to 8 grains of pepsin.

The regulation of the alkaline balance of the blood, and through it of the tissue fluids, is one of the most important functions of the kidneys. Treatment with hydrochloric acid largely regulates the amount and character of the urine excreted by its action on the renal tissue. Where acid is being administered in doubtful cases the blood pressure should always be observed to avoid overdose. —J. Campbell McClure and H. A. Ellis, *Lancet*, 11/1921, 271.

The role of hydrochloric acid in the causation of gastric pain. Concentrations of 0.5% or even less will reproduce typical gastric pain in susceptible individuals suffering from painful disturbances of gastric function. Hydrochloric acid plays no essential part in ordinary pain production —T. L. Hardy, *Lancet*, 1/1929, 711.

**Betainæ Hydrochloridum.**  $C_5H_{11}NO_2 \cdot HCl = 153.6$ .

(Betaine (*Syn.* TRIMETHYL-GLYCOCOLL.  $C_5H_{11}NO_2 = 117.1$ ) occurs in beets and mangolds (especially *unripe* roots) and has been found in a number of vegetable and animal substances. It is formed on oxidation of choline and is chemically related to muscarine and neurine.)

*Dose.*—1 to 8 grains (0.06 to 0.5 g.).

White crystalline substance soluble in water 1 in 2; in alcohol about 1 in 20.

*Uses.* Liberates hydrochloric acid (almost 25% of its weight), and is given with pepsin or diluted with water in gastric affections.

**Acidol** (*Bayer Products, London*). Betaine hydrochloride in  $7\frac{1}{2}$  gr tablets.

**Acidol-Pepsin** (*Bayer Products, London*)

*Dose*—1 to 2 tablets ( $7\frac{1}{2}$  grains in each) in water after meals

Contains betaine hydrochloride and pepsin. Issued in two strengths, No. 1 strongly acid, No. 2 slightly acid, equivalent to 10 and  $1\frac{1}{2}$  minims respectively of dilute hydrochloric acid.

In anorexia, hypochlorhydria, gastritis, etc.

**Acidulin** (*Eli Lilly, London*). Glutamic acid hydrochloride. Liberates free HCl in presence of moisture. Capsules contain the equivalent of 10 drops of dilute HCl. For use in the treatment of conditions exhibiting deficiency of gastric HCl.

**Betacid** (*Richter, London*). Betaine hydrochloride and pepsin.

**Paralactol** (*Homburg Pharma Ltd, London*). Betaine-glutamine hydrochloride in powder form for the treatment of gastric disturbances due to insufficiency of HCl.

**Ammonii Chloridum** (*B.P., U.S.P. XI, P. Helv. V, P. Dan.*).  $NH_4Cl = 53.50$ .

*Dose.*—5 to 60 grains (0.3 to 4 g.).

White crystals soluble 1 in 3 of water and 1 in 60 of alcohol (90%).

*Incompatible* with alkalis and carbonates of alkaline earths.

*Uses.* Mildly expectorant, diaphoretic and diuretic. Is administered to render the urine acid in the treatment of urinary infections, e.g., with mandelic acid; change of pH alone has no effect on bacilluria. By inhalation of the vapour (Vapor Ammonii Chloridi) generated by interaction of hydrochloric acid and ammonia, it is used to increase secretion in bronchitis, pharyngitis and in affections of the Eustachian tube.

**NEPHRITIS.**—Where ingestion of calcium chloride causes nausea and vomiting, ammonium chloride in doses of 5 to 16 g. for 3 to 18 days may be substituted with practically identical results. Watch for acidosis —P. S. Hench, *J. Amer. med. Ass.*, 11/1926, 13.

**SPASMOPHILIA (INFANTILE TETANY).**—Ammonium chloride, 5 g. a day, efficacious, but effect only transient. Must be followed up by specific measures against tetany.—Dan T. Davies, *Lancet*, 1/1930, 202.

**URINARY AFFECTIONS**—In cases of infection with the proteus bacillus, ammonium chloride would seem to be unsuitable as a urinary acidifier for biochemical and bacteriological reasons. In treating infections of the kidneys with the proteus bacillus, systemic acidification may be dangerous and lead to the formation of new stones, unless one is successful in obtaining a strongly acid urine. This may be due to the rapid manufacture of ammonia by the proteus bacilli—R Chute, *New Engl J Med*, 1/1936, 869. See also D M Lyon and D M Dunlop, *Brit med J*, 11/1937, 1096.

**Collyrium Ammonii Chloridi (B P C).** 0.5% w/v.

**Lot. Evap. Meth. (N I F)**

Industrial methylated spirit 1 oz, ammonium chloride 2 dr, water to 8 oz

[P1] **Mist. Ammon. Chlorid. Co. (N I F)**

Ammonium carbonate 3 gr, ammonium chloride 5 gr, tincture of chloroform and morphine 5 m, liquid extract of liquorice 5 m, water to  $\frac{1}{2}$  oz

**Pastilli Ammonii Chloridi (B P C)** contain 2 gr (0.13 g)

**Pastilli Ammonii Chloridi Compositi (B P C)** contain 2 gr. of ammonium chloride and 2 m. of liquid extract of liquorice.

**Trochisci Ammonii Chloridi (T H)** 2 grains, marked "MA". One every 3 hours useful in congestion of the pharynx and larynx, loss of voice arising from cold and bronchial cough.

**Trochisci Ammonii Chloridi Compositi (B P C) Syn.**

TROCHISCI AMMONII CHLORIDI ET GLYCYRRHIZÆ

Contain 3 gr. of ammonium chloride and 3 gr. of extract of liquorice. **Tablets** are also made same strength.

**Trochisci Ammonii Chloridi Compositi (T H)** Contain ammonium chloride 1 gr, potassium chlorate 2 gr, and  $\frac{1}{4}$  gr approximately of cubeb. Marked "CMA".

**Calcii Chloridum (B P, F E VIII).**  $\text{CaCl}_2 = 111.0$

**Dose**—Per os, 10 to 30 grains (0.6 to 2 g). The B P Add. states that when calcium chloride is prescribed for injection hydrated calcium chloride shall be dispensed.

This is the anhydrous salt, the B. P. requiring not more than 10% of water. In fused white agglutinated very deliquescent masses.

**Soluble** 1 in  $1\frac{1}{2}$  of water, 1 in 3 of alcohol 90%

**Calcii Chloridum Hydratum (B P Add., P Helv V, P. Dan, P. Belg IV, P. Ital V, P Jap IV)**  $\text{CaCl}_2 \cdot 6\text{H}_2\text{O} = 219.1$ .

**Dose.**—By intramuscular injection, 1 to 3 grains (0.06 to 0.2 g.); by intravenous injection, 10 to 30 grains (0.6 to 2 g.).

Intravenous injection of 4 ml. of 10% solution dangerous—believed to cause heart-block—W. D M Lloyd, *Brit med J*, 1/1928, 664.

In colourless deliquescent crystals with slightly bitter taste, containing about 50% of  $\text{CaCl}_2$ .

**Soluble** 4 in 1 of water, 1 in 1 of alcohol 90%.

**Incompatible** with carbonates, phosphates, sulphates and tartrates.

**Uses.** Calcium chloride increases the coagulability of the blood, and so acts as a hæmostatic.

It is employed in itching skin affections, e.g., pruritus, prurigo, urticaria. It is useful in chilblains, full dose frequently, and certain forms of headache. In tubercular disease, chorea, glandular affections, to stop the growth of uterine fibroids, and to check the vomiting due to sarcinæ.

**Metabolism.**—Daily calcium requirement of growing boys found to be 0.43 g. When an individual is living on a low calcium diet the amount of calcium in the blood may not necessarily reflect the deficiency—J M Henderson, *Lancet*, 11/1930, 755

Importance of calcium metabolism—G Arbour Stephens, *Brit med J*, 1/1931, 605

Studies in calcium and phosphorus metabolism—Donald Hunter, *Lancet*, 1/1930, 897, 947, 999, 1022

The free or floating calcium added by means of milk to a nursing mother's diet is of intense value, both to mother and child. In addition, as calcium phosphate has to be formed, the phosphorus-calcium ratio must be correct. The calcium of the diet should be 0.63 g (minimum total calcium *per diem* 0.9 to 1 g, and of phosphorus 0.88). In treatment of tuberculosis calcium to be given to promote calcification—F E Tylecote, *Med Pr*, 1929, 261

Significance of blood calcium. About 60% of the calcium in the blood is in a diffusible form, the rest is probably combined with protein. When food ingested is free of calcium, tetany occurs. Hypocalcæmia occurs in spasmodophilia, rickets, renal dwarfism, celiac disease, osteomalacia, parathyroidectomy, and renal disease—Dan T Davies, *Lancet*, 1/1930, 149

An interesting discussion on the therapeutic uses of calcium salts at the meetings of the B M A 1927—*Brit med J*, 11/1927, 777 *et seq*

ACNE—A 10% solution of calcium chloride intravenously, 5 ml every third day, increased to 10 ml every second day, of value. Inject slowly, taking care not to infiltrate the skin or the hypoderm. When patient complains of heat in the face, stop till this disappears—*Per Prescriber*, 1929, 332

ANEURISM OF THE AORTA (abdominal) apparently cured by calcium chloride in doses of 15 to 30 grains—Whitla, *Pract Med*

ANGIONEUROTIC OEDEMA treated with 10 grain doses thrice daily, increasing to 20 grains. The swellings which appeared continuously in different parts of the body disappeared completely

CANCER OF THE BUCCAL CAVITY—For the prevention of pneumonia after operations on the tongue and mouth for cancer. For about a week before operation give 15 gr calcium chloride thrice daily (practically all cases of cancer are deficient in calcium), rinse the mouth with a good antiseptic or pure alcohol, with caution against swallowing mouth-wash, and for 3 days after operation give 10 ml antistreptococcus serum hypodermically. 100% success—James Barr, *Brit med J*, 1/1934, 452

CHILBLAINS—Calcium consumption helps to an extent—*Brit med J*, 1/1931, 516

Coagulation-time of blood not delayed in chilblains—R Hallam, *ibid*, 215

Calcium chloride, 10 grains three times daily, and parathyroid  $\frac{1}{4}$  grain once or twice. The lactate is not so good—E A Milner, *Brit med J*, 11/1926, 917

CHORIA—There is a rather low total serum calcium content. The calcium content of the cerebrospinal fluid is consistently low—E C Warner, *Lancet*, 1/1930, 339

DYSENTERY—Excellent results with injections of 10 ml of a 10% solution of calcium chloride with morphine, subcutaneously—*J Amer med Ass*, 11/1925, 1521

ECLAMPSIA—Calcium therapy is the prophylactic. Continuous administration during pregnancy of 15 gr calcium phosphate in  $\frac{1}{4}$  oz of water thrice daily as prophylactic in midwifery, combined with a 1 in 1000 solution of acriflavine in glycerin (*qv*) for vaginal injection—J L Moor, *Brit med J*, 1/1931, 118

Calcium therapy in eclampsia disappointing. The fits are not influenced by the calcium content of the serum—W C W Nixon, *Lancet*, 11/1931, 292

ECZEMA treated with a 6% calcium chloride ointment, found to be effective—G Lampronti, *per Pharm J*, 1/1923, 573

EPIDIDYMITIS well treated by intravenous injection of 0.5 to 1 g in dilute solution—4 or 5 injections, one daily—*Per J Amer med Ass*, 11/1928, 1136

ERYTHEMA NODOSUM.—Cured by calcium chloride with local sedatives and rest—H Hallam, *Brit med J*, 11/1921, 917

HÆMATEMESIS OF GASTRIC ULCER—In severe cases the only reliable drug is calcium chloride, 1 dr dissolved in 5 or 6 oz of water given by the rectum, alone or in conjunction with saline transfusion or subcutaneous injections—Whitla, *Pract Med*

**HÆMOPHILIA** treated intravenously, 10 to 12 injections of 20 ml of 5% solution --*Paris Med*, Dec, 1924, 467, per *Prescriber*, 1926, 23

**HÆMORRHAGE** controlled by intramuscular injection of calcium chloride 1 gr in 100 m injected *deeply* into the gluteal muscles is generally painless. The calcium value of the blood is found to rise slowly to a maximum in 6 hours and then to remain constant for 24 hours. The effect is probably a direct one on the blood vessels. The increased calcium content of the plasma may cause combination between the calcium and the blood lipoids with consequent acceleration of clotting. A second injection at end of 24 hours and a third, 24 hours later, may be given. *Per os*, calcium salts have no effect on blood calcium. Helpful in uterine hemorrhages and results in aneurisms hopeful.—W R Grove and H W C Vines, *Brit med J*, 11/1921, 40

**HÆMORRHAGES, INTESTINAL**, to check, 30 to 60 gr daily have been given orally, accompanied by rectal injections containing 60 grains to two pints of water, opium may be given in addition

**HAY FEVER**—Consumption of large quantities of flesh increases the excretion of calcium. A low body content of calcium is favourable to hay fever, the administration of calcium chloride acting beneficially. A retention of potassium and a greater output of sodium results from increased calcium in the diet.—*J chem Soc Abstr*, 1/1922, 1210. 10 grain doses *t d* have been advised

**JAUNDICE** 5 ml of 10% solution intravenously helped to hasten coagulation of the blood, prevent post-operative bleeding, and neutralise toxic bile products --*J Amer med Ass*, 11/1925, 885

**NEPHRITIS** and **EDEMA** successfully treated with calcium chloride, 2½ to 4½ dr daily, free diuresis occurring --*Brit med J Fpit*, 11/1924, 62

In chronic parenchymatous nephritis the calcium is at a low level—Dan T Davies, *Lancet*, 1/1930, 203

**PLEURITIC EFFUSION**—Calcium chloride *per os* found to have remarkable effect in treatment. 30 g of the dry granulated salt (*Caution* an extraordinary dose!) in 100 ml of water taken in a little coffee and milk the best method of administration --*Per Practitioner*, 11/1923, 233

**PNEUMONIA, ACUTE LOBAR**, has been treated with 5 to 15 gr doses every 4 hours

**TETANY**—Intravenous injection of 10 ml of a 10% solution of calcium chloride is an excellent emergency measure for the relief of symptoms of parathyroid tetany. A good method of treatment is to give orally a large amount of calcium chloride (150 grains daily), where this is not effective, and where ichthyuria is present, give 50 to 100 ml of N/3 hydrochloric acid in milk (1 of acid to 20 of milk) to increase absorption of the calcium —D Campbell, *Lancet*, 1/1935, 372

In acute cases of spasmodic tetany the calcium content of the serum ranges between 4 and 8 mg per 100 ml. Give calcium chloride 2 g every 2 hours. As much as 6 g can be given in 24 hours in milk to an infant without any apparent intolerance. Improvement in ½ hour. Hydrochloric acid (e.g., 260 ml of N/10 acid with 750 ml of milk) and ammonium chloride, 5 g a day, also efficacious but they are only transient in effect —Dan T Davies, *Lancet*, 1/1930, 202

**TUBERCULOUS DIARRHŒA** has been treated by calcium chloride *intravenously*, e.g., 5 ml doses of 5% solution with benefit. Ascribed to the action on the sympathetic system, checking peristalsis. —*Prescriber*, 1919, 202. *The tolerance of the patient should invariably be ascertained before administering the full dose*

Tuberculous intestinal ulcers healed by weekly intravenous injections of 5 ml of 5% solution for 102 weeks --*Amer Rev Tuberc*, Sept, 1925, per *J Amer med Ass*, 11/1925, 1583

Calcium chloride intravenously is excreted in the urine to the extent of about 50% in 3 hours and is completely excreted in the urine and faeces in 3 days. It is impossible to bring about retention of calcium in tuberculous patients even by a series of injections at short intervals —*Biochem Z*, 1926, 146, per *Brit chem Abstr. (A)*, 1926, 753

Intravenous injections should not exceed 1% strength. 50 ml doses given slowly —*J trop Med (Hvg)*, 1925, 386.

In tuberculous diarrhœa give calcium chloride ½-1 gr intramuscularly or intravenously at intervals of 2 or 3 days with bismuth carbonate *per os*, say 1-2 dr thrice daily. Injections should be continued for 2 or 3 weeks —F Savy, *Lancet*, 11/1925, 674, 781

**Mistura Calcii Chloridi (N I F)**

Calcium chloride 10 gr, syrup of ginger  $\frac{1}{2}$  dr, water to  $\frac{1}{2}$  ounce

**Mistura Calcii Chloridi Albuminata (B V H)**

Calcium chloride 15 gr, solution of pectin 2 dr, syrup 30 m, water to 1 oz  
(Solution of pectin contains pectin (100 grade) 87.5 gr, glycerin of chlorbutol (1 in 12)  $\frac{1}{2}$  oz, water to 20 oz)

A calcium mixture for oral administration over long periods to asthmatic and arthritic patients, it does not cause derangement of the stomach—*Pharm J* 11/1934, 620.

**Syrupus Calcii Chloridi (B P.C.) Syn ELIXIR CALCII CHLORIDI.**

**Dose.**—1 to 2 drachms (2 to 4 ml)

Calcium chloride 1 in 8 in distilled water and syrup of lemon

**Afenil** (*Knoll, Ludwigshafen, Pharmaceutical Products, London*) A double combination of calcium chloride and urea in 10% solution for intravenous calcium treatment in hay fever, bronchial asthma, rhinitis, influenza, hæmorrhage etc

**Calcosol** (*Richter, London*) Solution of calcium chloride and urea for intravenous injection. In 1 and 5 ml ampoules (10 and 20%) **Dose**—3 to injections weekly. In hæmophilia, hæmoptysis, etc

**Transkutan** (*Transkutan-Gesellschaft, Berlin*) A proprietary containing calcium chloride, iodine, bromine, strontium and lithium salts, and radium with aromatic oils, for adding to baths. In rheumatoid arthritis fibrositis, etc

**Magnesi Chloridum (B P.C., P Helv V)**

$\text{MgCl}_2 \cdot 6\text{H}_2\text{O} = 203.3$

**Dose**— $\frac{1}{4}$  to 1 ounce (8 to 30 g)

Deliquescent crystals, **soluble** about 2 in 1 of water and 1 in 1 of alcohol 90%. Mild purgative, a dose in  $\frac{1}{2}$  pint of hot water useful for constipation and in dyspepsia and stomach disorders

War wounds have been treated with 1.2% solution.

**Delbiase** (*Phargene, London*) Tablets contain magnesium chloride 9.135 gr, with small amounts of magnesium iodide, bromide and fluoride **Dose**—2 to 4 tablets daily. In asthenia, etc, and in numerous skin affection (4 tablets daily)

**Potassii Chloridum (B P.C., P Helv V, P Dan).**

$\text{KCl} = 74.55$

Has been advocated for use in place of table salt by gouty and rheumatic individuals, and for increased arterial pressure. Olive found a tendency to indulge in the use of salt in advancing age (over 65). When potassium is ingested in excess of sodium, a loss of the latter takes place from the system. The following is better to taste.—

**Pulvis Potassii et Sodii Chloridi Compositus**—*Oliver* Potassium chloride 16, sodium chloride 8, lithium benzoate 1. A half-drachm measureful to be taken

**Table Salt** containing 50% each sodium and potassium chloride, to automatically supply potassium salts lost in the preparation and cooking of food. Apart from the problematical relation of potassium deficiency to cancer, potassium is a valuable addition to dietary and effective in preventing gout and rheumatism—*F S Rose, Pharm J*, 11/1926, 411

**MYASTHENIA GRAVIS**—Potassium chloride given in large doses, 10 to 12 g, b the mouth, gives a demonstrable improvement in myasthenia. Six patients have taken the salt daily for two months in doses of from 4 to 6 g six times a day—the largest total in one day being 40 g, and this treatment has proved a valuable adjunct to Prostigmin (*q.v.*). The only unpleasant symptom has been a mild diarrhoea and some nausea following the larger doses—*L. P. E. Laurent and W. W. Walther, Lancet*, 1/1935, 1434.

**Sodii Chloridum** (*B P., U.S P. XI, P. Dan.*).  $\text{NaCl} = 58.45$

*Dose.*—10 to 60 grains (0.6 to 4 g.). White cubical crystals.

(**Natrium Chloratum** (*P.G. VI, P. Helv. V*) is sodium chloride. Sodium chlorate,  $\text{NaClO}_3$ , is called **Natrium Chloricum** in Germany)

**Soluble** 1 in about 3 of water (not more in boiling water), about 1 in 200 of alcohol 90%, about 1 in 10 of glycerin

**Uses.**—Although in common use is not requisite to those having ordinary mixed diet, but is necessary to vegetarians. Insufficient salt leads to anæmia, debility and œdema of face and ankles. Large doses are emetic

As a purgative may be given in dose of 120 to 240 grains. As a laxative, 75 grains in a tumbler of cold water, it is stated, acts efficiently and without pain. Rectal injections are used to kill threadworms. Hypodermically or into the veins as normal saline solution, *q.v.*

In large doses, 10 to 15 g. daily, sodium chloride is frequently of considerable value in the treatment of Addison's disease and may substantially reduce the dose of suprarenal cortex extract required. In some cases its administration may replace treatment with cortical extract, especially if the potassium intake is kept low.

**ADDISON'S DISEASE**—Striking results in a case from a dosage of 15 g. a day. The sodium in the blood is reduced in cases of Addison's disease—G. Graham, *Lancet*, 11/1933, 1446

Dramatic effect in a case put on 10 g. daily (in milk), relapse following reduction of dose to 5 g. daily. Treatment with sodium chloride is not in any way curative, but by supplying an excess of sodium makes good the wastage—C. M. H. Howell, *Lancet*, 1/1934, 1116. See also R. F. Loeb, *Proc Soc exp Biol Med*, N. Y., 1933, 0, 808, W. G. Sears, *Lancet*, 1/1934, 950

Even if the intake of potassium is no higher than that provided by an ordinary diet (4 g. or more), as much as 18 g. of sodium chloride may not prevent the development of crisis, with a low potassium intake (1.6 g. or less), symptoms may be slow in developing, or even indefinitely postponed. Patients otherwise requiring cortical hormone may be maintained in good condition by administration of sodium salts only if the potassium is restricted—R. M. Wilder and co-workers, *Proc Mayo Clin*, 1936, 2, 3

#### **Dechlorination or Salt-free Diet.**

**NEPHRITIS** has been treated by this (in many forms of nephritis the kidneys fail to eliminate salt). Copious diuresis sets in, œdema disappears and remains more or less absent so long as the treatment is kept up. Food should be cooked without it. The salt-free diet is, however, often disappointing. It should be tried where heart and lungs are hampered by excessive œdema, and in migraine and chlorosis. The theory of salt retention does not, however, wholly explain œdema following gastro-enteritis in children nor all cases of œdema in Bright's disease

**EPILEPSY** has been treated by sodium chloride reduction. Reduce the salt in the diet and the absorption of bromide will increase. The combined treatment, e.g., with bromide tablets containing 2 gr. of salt and 18 gr. of bromide to be used to salt broth, is satisfactory

Carbohydrates increase the retention of water while fats diminish thirst. If no salt be added to the food the body loses 15 to 25 g. of sodium chloride and  $1\frac{1}{2}$  to  $2\frac{1}{2}$  kilos of water, a saltless diet is therefore itself diuretic. Generally speaking, the intake of water and salt increases the quantity of water taken up by the tissues and consequently may cause œdema—P. E. Morhart, *Brit med J. Fmt*, 1/1926, 86

**Cerebos Salt** (*Cerebos Ltd, London*) Sodium chloride with phosphates, mostly calcium phosphate, less deliquescent than "salt." Is intended to replace the phosphates removed in the preparation of food and to prevent the salt becoming moist



See also **Table Salt containing 50% Potassium Chloride** under Potassium Chloride

**Selarom** (Bayer Products, London) Mixture of calcium, magnesium, and sodium salts of organic acids. For salt-free dietary.

**Balneum Sodii Chloridi (B P C)** Contains 7 lbs of sodium chloride per 30 gallons. A tonic and stimulant, *e.g.*, in chronic rheumatism

**Collunarium Plasma (B V H)**

Sodium chloride 6 dr, sodium sulphate 2 dr, sodium phosphate 2 dr, sucrose 3 oz. (Apoth) or tragacanth 20 gr, thymol 3 gr, menthol 3 gr, alcohol 90% 1 dr, distilled water to 6 oz

**Hustus Sodii Chloridi Compositus (Mid H)**

Sodium chloride 5 gr, sodium bicarbonate 5 gr, spirit of chloroform 5 m, caraway water to 1 oz. For the dry cough of the early stages of acute bronchitis

**Liquor Sodii Chloridi Physiologicus (B P)** *Syn* PHYSIOLOGICAL SALINE SOLUTION, NORMAL SALINE SOLUTION

A sterile 0.9% *w/v* aqueous solution of sodium chloride. *U S P XI* has 0.85%, and *Fr Cx Supp*, 1926, 0.8%.

This is isotonic with the liquid of the blood corpuscles and possesses the same osmotic pressure as the liquor sanguinis, it has a freezing point of approximately  $-0.56^{\circ}$ . The injection should be made at least at  $105^{\circ}\text{F}$  (*this is important*), into any convenient vein. The rate of injection varies, it may be as rapid as a pint in 10 minutes, or as slow as 8 ounces per hour (see refs *infra*)

Fortunately only an approximation to an isotonic solution is necessary, as mucous membranes are practically insusceptible to changes in osmotic pressure within fairly wide limits. The solution should be slightly alkalisied. 0.1% sodium bicarbonate is sufficient.—Marshall

**Isotonic Sodium Chloride** for ophthalmic use is 1.4%.

Rules for isotonic solutions.—*Pharm J*, 1/1929, 325, see also *ibid.*, 1/1934, 633, and *B.P.C.*, p 1283

The lachrymal secretion is stated to contain 1.3% of sodium chloride and 0.5% of albumin. Eye lotions are often made isotonic.

**Uses.** Physiological saline solution is largely employed in surgical shock by intravenous and rectal injection, also in post-partum hæmorrhage. Particularly useful in the hæmorrhage of typhoid. Aids recovery from poisoning by phenol, morphine and alcohol. Given per rectum or subcutaneously in the recurrent vomiting of infants. Cholera, pneumonia, uræmia, relapsing fever, delirium tremens, tetanus and diphtheria have been well treated by subcutaneous and intravenous use.

Continuous intravenous saline preferable to putting into the circulation a pint or more of fluid comparatively suddenly. The cannula (preferably gold-plated) is tied into a vein a little larger than itself, either in the back of the hand or the saphena or one of its branches, just below the knee, or the vein just in front of the internal malleolus, the vein being exposed by a transverse incision after infiltration anæsthesia. The cannula and wound should be moist with citrate solution at time of introduction. A splint is used to keep the limb at rest. The fluids generally used are normal saline or 5% glucose in normal saline, kept warm by placing an electric heating pad on the limb over the cannula. The average rate of flow for an adult is 50 drops per minute ( $\frac{1}{4}$  pint an hour), increased to 100 drops in the first hour if necessary (œdema the signal for reducing flow). May be continued for 3 to 7 days.—V Bailey and J M Carnow, *Brit med J*, 1/1934, 11. Value confirmed by E R Flint, *ibid.*, 75, W Morris, *ibid.*, 75. In almost constant use at the Northampton General Hospital since June, 1931. B L Laver, *ibid.*, 123

**ACNE** —Intravenous injections of 100 ml increased by 50 ml until a maximum of 250 ml was reached (unless the patient had only one or two pus pockets, when the solution was injected locally into the pus and around the inflammatory base), most serviceable in pustular acne and furunculosis —H Goodman, *Arch Derm Syph*, June, 1935, 828

**GONORRHOEA** —1% saline solution has many advantages over a 1 in 10,000 potassium permanganate solution for posterior irrigation —*Brit med J Epit* 11/1929, 43

**INFUS** —As in cholera, there is dehydration Give  $2\frac{1}{2}$  to  $3\frac{1}{2}$  pints of normal saline intravenously —D C Corry, *Brit med J*, 1/1931, 219

**RETAINED PLACENTA** —The rapid injection of 350 to 400 ml of saline into the umbilical vein in cases of retained placenta is a successful and much less dangerous undertaking than the manual removal of this organ —David Levi, *Practitioner*, 1/1936, 508

**SURGICAL SHOCK** —Saline fluid injected to the extent of 300 ml per kilo causes embarrassment and failure of respiration When the causes of shock are active an injection of fluid cannot force recovery —J D Malcolm, *Med Pr*, 1922, 420

Instead of saline injections, gum saline-Bayliss (sodium chloride 2 g, potassium chloride 0.05 g, calcium chloride 0.05 g, acacia 5 g, distilled water 100 ml) is advocated for loss of blood if actual blood transfusion is impossible —H Pritchard, *Brit med J*, 1/1927, 793 See *Acacia*

**Solvellæ Sodii Chloridi (B P C)** contain 20 gr (1.3 g)

**Ringer's Solution (B P C)** Sodium chloride 0.7, potassium chloride 0.014, calcium chloride 0.012, sodium bicarbonate 0.02, water to 100 Is isotonic with the serum of frog's blood

**Ringer-Locke Solution (B P C)** Sodium chloride 0.9, potassium chloride 0.042, calcium chloride 0.024, dextrose 0.1, sodium bicarbonate 0.05, water to 100 Is isotonic with the serum of mammalian blood

**AURICULAR FIBRILLATION** —There is always calcium deficiency Ringer's solution containing about double the usual amount of calcium chloride and 2 ounces of syrup of glucose to the pint is a good drink which should be drunk freely —Sir J Barr, *Brit med J*, 1/1930, 774

**MENTAL DISEASES** —In certain mental diseases in which there is a toxic element a litre of Ringer-Locke injected twice weekly —J P Steel, *Brit med J*, 11/1927, 1177

**Ringer-Tyrode Solution (B P C)** Sodium chloride 0.8, potassium chloride 0.02, calcium chloride 0.02, magnesium chloride 0.001, dextrose 0.1, sodium acid phosphate 0.005, sodium bicarbonate 0.1, water to 100 Is isotonic with the serum of mammalian blood

**Fischer's Modified Ringer's Solution.**

Sodium chloride 0.5, calcium chloride 0.04, potassium chloride 0.02, distilled water to 100 This is employed in surgical practice instead of normal saline, e.g., for dissolving procaine Has advantages over Ringer's or Tyrode's solution This solution possesses constant pH value of 7.52 at 37°, is isotonic with blood, is sterilisable and contains calcium and potassium in a ratio approximating to that in arterial blood Similar relation exists between total uni- and bivalent positive ions

**STOCK SOLUTION** contains sodium chloride 10.5 g, potassium chloride 0.5 g, magnesium chloride 0.1 g, calcium chloride 0.3 g, N/1 phosphoric acid 5 ml, and 50 ml of water.

For use filter 50 ml and add 1 litre of water, heat and when cool saturate with oxygen, and add 5 ml of sterile N/1 sodium carbonate solution —*J chem Soc Abstr.*, 1/1922, 964

**Steriles of Ringer's and of Locke's Solutions (Martindale, London)** contain sufficient to produce 1 litre of the respective solutions on dilution

**Hypertonic Saline Solution.**—Sodium chloride 5% in distilled water with  $\frac{1}{4}$ % of sodium citrate added (the proportion is sometimes varied up to 10% of salt and 1% of sodium citrate) *St. G.H.* is 5% without citrate

**ACUTE INTESTINAL OBSTRUCTION** well treated immediately after operation by 20 g of sodium chloride intravenously in 10% solution 30 ml at a time during 48 hours (maximum 70 g for a man of average weight) with 1 litre physiological serum subcutaneously during the same period—*Brit med J. Epit*, 1/1928, 32.

Discussion at B M A Centen Meeting, 1932 *Sir W I de C Wheeler*—Hypertonic saline intravenously reduced mortality rate from 50 to 11% *D. P D Wilkie*—Fluids and chlorides must be given liberally before operation *R Graham* (Toronto)—Thousands of ml of saline necessary in these cases.—*Brit. med. J*, 11/1932, 364.

**CARBUNCLES**—No carbuncle has been incised, excised or scraped during the past three years in the special wards devoted to the treatment of acute surgical infection at the London Hospital, the total number of carbuncles treated being 78. The local application employed is a fomentation or compress of fluffed-up white gauze well wrung out of a hot solution of hypertonic salt—one ounce to the pint—renewed two-hourly during the day and four-hourly at night. In a few days the slough comes away entirely, when dry fluffed gauze dressings are substituted. The method is equally applicable to boils. In infections of the face, nose and lip the part is bathed in the hypertonic salt solution for a quarter of an hour at a time at two- or three-hourly intervals, a compress being applied as near as possible during the intervals—*C Donald, Brit med J*, 1/1935, 963

**DIPHTHERIA**—Adrenal failure may play a part in fatalities from toxic diphtheria, the blood-serum sodium is always lowered in diphtheria. Many cases with a very poor prognosis have made a satisfactory recovery after being given continuously per rectum a 5% solution of glucose in normal saline during the acute stage, or a daily intravenous injection of 30 ml of a 5% hypertonic salt solution—*A Maclean, Lancet*, 1/1935, 699.

**POST-CONCUSSIONAL STATES.**—One of the effects of injecting hypertonic saline into the circulation is a diminution in the volume of the brain—hence of use in post-concussional or post-concussional states—for relief of headache—even 100 ml. of 30% solution can be given, but usually 50 ml of 15% effective—*A Feiling, Brit med J*, 11/1930, 907.

**TRICHOMONAS VAGINITIS**—Vaginal douching with 25% salt solution gives prompt relief and in most cases prevents recurrence. The effect is due to osmotic action, and is non-irritating and inexpensive—*L Rosenthal and co-workers, J. Amer med Ass*, 11/1935, 105

**VARICOSE VEINS** have been treated by injection with strong saline as sclerosing agent

Large amounts may be injected, 10 ml for one injection, up to 20 or 30 ml at one time, or with 5 or 10 ml, 3 or 4 injections at one sitting. A more adherent and exclusive thrombosis and a better end-result than with other agents

Sodium chloride 20% the "safest as far as systemic reaction is concerned" Retards clotting of the blood, and incapable of giving rise in the ordinary way to any thrombosis, either at time of injection or subsequently. Probably the most efficient and safest to use and will remain so until the ideal solution is discovered—*T. H. T Barber, Brit med J.*, 1/1930, 219, *ibid*, 11/1930, 60

4 to 10 ml of 20% solution gives good results, but is not certain in its effects and causes cramp-like pains—*A H Douthwaite, "Injection Treatment of Varicose Veins"* (H. K. Lewis).

**Varicophytin** (*Napp, London*) Sterile hypertonic sodium chloride solution with an anæsthetic. For the injection treatment of varicose veins.

**Hypotonic Saline Solution** (*St. G H*) is 0.3%.

[P2] **Cheron's Serum.**—Sodium chloride 2, phenol 1, sodium phosphate ( $\text{Na}_2\text{HPO}_4$ , called neutral phosphate in France) 4, sodium sulphate 8, distilled water to 100.

**Enema Sodii Chloridi** (*B P C*) *Dose*—20 ounces (600 ml) 2.5 to 5% *w/v* in mucilage of starch or in 5% *w/v* aqueous soft soap. Hypertonic enema—4% *w/v* in water

**Pulv. Hypertonic (N.I.F.)**

Sodium chloride 4, sodium citrate 1 Two heaped teaspoonfuls to be dissolved in  $\frac{1}{2}$  pt of warm water

**Trunecek's Serum** for nervous ailments and high arterial tension

*Dose.*—Subcutaneously 1 ml to commence with, increasing by 0.2 ml May also be given by rectum and mouth

Sodium chloride 492, sodium sulphate 44, sodium phosphate 15, sodium carbonate 21, potassium sulphate 40, water to 10,000

**Tablets of Trunecek's Serum** are prepared 5 grains each, *i.e.*, equivalent approximately to 5 ml of the serum *Daily dose* 3 to 6 with meals Administration *per os* is equally effective.

For atheroma and sclerosis of arterial coats

Trunecek's Serum has a freezing point of 3.29°, and an osmotic pressure 5.875 times greater than blood serum—*i.e.*, it is strongly hypertonic.

**Sea Water.**

Schweitzer's analysis is as follows Sodium chloride 2.7059, potassium chloride 0.0765, magnesium chloride 0.3667, magnesium bromide 0.0029, magnesium sulphate 0.2296, calcium sulphate 0.1407, calcium carbonate 0.0033, water to 100—*Chem. & Drugg.*, 1/1930, 88

**Artificial Sea Water.**—The following has been advised for injection as enema—

Sodium chloride 27, magnesium chloride 3, potassium chloride 1, magnesium sulphate 14, calcium sulphate 1, distilled water to 1000

**Sea Salt.** *Syn.* BAY SALT, CITEAN SALT

Obtained from sea water, which contains about 2.7%. In warm countries, the water is allowed to evaporate in the air, and in cold countries it is allowed to freeze, when the ice is removed and the mother liquor then evaporated.—*Chem. & Drugg.*, 1/1930, 88

**Pulvis Sodii Chloridi Compositus.**

Sodium chloride 6, potassium chlorate 1, alum 1, boric acid 1, borax 6. A saltspoonful in a half tumbler of warm water as a gargle is very beneficial for inflamed conditions of the throat

**Unguentum Sodii Chloridi (St. B. H.)** *Syn.* UNGUENTUM SALVAS (R.V.I.)

Sodium chloride and soft paraffin, equal parts R.N.H. has sodium chloride 1, sodium bicarbonate 1, soft paraffin to 4

Ringworm (of hairy regions) Croton oil treatment is painful Use this ointment instead Rub in daily, after bathing the head with very hot water Even more painful than croton oil—A. Whitfield, *Lancet*, 1/1923, 1124.

[P2] **Acidum Hydrofluoricum.** HF = 20.0 *Syn.* FLUORIC ACID.

[P1] "*Alkali fluorides other than those specified in Part II of this list.*"

[P2] "*Hydrofluoric acid, potassium fluoride; sodium fluoride; sodium silicofluoride*"

[B3] "*Sodium fluoride—in substances containing less than 3% of sodium fluoride as a preservative*"

[B3] "*Sodium silicofluoride—in substances containing less than 3% of sodium silicofluoride as a preservative.*"

Manufactured by the action of sulphuric acid on fluor spar ( $\text{CaF}_2$ ) in lead or platinum vessels, and redistilled for medicinal use. It contains about 40% *w/w* of the gas and emits suffocating fumes. It attacks glass and must be kept in gutta-percha bottles, or bottles coated internally with ceresin or hard paraffin

**HYDROFLUORIC ACID BURNS.**

Relief from use of copious quantities of dilute ammonia solution followed by ice bath, also, in severe and extensive burns, subcutaneous injection of 10% ammonium chloride solution relieves pain and prevents extension. In from 24 to 48 hours, the areas that have come in contact with acid appear white and lifeless. These areas should be extensively debrided and the white surface tissue removed (this causes no pain). Wet magnesium sulphate dressings are then applied for a few days and subsequently bland ointment dressings. This

procedure relieves pain, hastens healing and reduces scarification - F. E. Evans, *J. Amer. med. Ass.*, 11/1932, 1194

[P2] **Acidum Hydrofluoricum Dilutum.**

**Dose.**—5 to 15 minims (0.3 to 1 ml). Contains about 0.5% of the strong acid. Even thus diluted should not be kept in glass bottles for use. Has been given for goitre.

[P2] **Sodii Fluoridum (B.P.C.)**  $\text{NaF} = 42.00$

**Dose.**— $\frac{1}{12}$  to  $\frac{1}{2}$  grain (0.005 to 0.03 g), in very dilute solution. Lustrous cubes or crystalline powder.

**Soluble** 1 in 25 of water, insoluble in alcohol.

**Antidotes.** Wash out the stomach, using lime water or a dilute solution of calcium chloride freely, or give 20 to 30 gr. of calcium chloride or lactate dissolved in water, and then an emetic. The dose of calcium salt should be repeated, or calcium chloride may be given intravenously. Keep patient lying down and warm. Give a purgative dose of castor oil. Demulcent drinks freely. Morphine,  $\frac{1}{4}$  gr. hypodermically, if necessary.

Calcium compounds effective in treatment of fluoride poisoning - Sharkey and Simpson, *J. Amer. med. Ass.*, 1/1933, 100.

Recovery after taking 5½ gr. in the form of an insect powder, mistaken for flowers of sulphur. Sickness, vomiting, diarrhoea, pains in legs and arms, dysphagia, and ocular paralysis with diplopia supervened. Oxygen and stimulants were administered, and later Coramine, strychnine, atropine and radiant heat. R. D. Bell, *Brit. med. J.*, 1/1936, 886.

For references to chronic fluorine poisoning see Vol. II.

**Uses.** Antiseptic in phthisis, also given in toxic goitre in doses of 1 dr. of 2% w/v solution three times a day with potassium iodide. Given hypodermically as 0.5% w/v solution. Mixed with meal is a specific for killing beetles and cockroaches. The aqueous solution attacks glass slowly.

**GRAVES' DISEASE.** 5 ml. of a 2% solution *intravenously* on alternate days. *Orally* 2.5 cg. in pill form. Malaise disappears, pulse rate reduced, weight increases, and B.M.R. lowered. Both exophthalmos and thyroid enlargement are ultimately much reduced or become unnoticeable. No contraindications and no danger - L. Goldemberg, per *Brit. med. J. Fpt.*, 1/1934, 55.

Sodium fluoride does not inactivate thyroxine *in vivo*, but its therapeutic use in hyperthyroidism is not condemned by this finding, since it may have an inhibitory action on the thyroid gland itself - M. H. Seevers and H. A. Braun, *Proc. Soc. exp. Biol.*, N.Y., 1935, 33, 228.

[P1] **Mistura Sodii Fluoridi (B.P.H.)** **Dose.**—1 dr. of A with 1 dr. of B.  
A.—Solution of sodium fluoride (2%) 30 m., aqueous solution of iodine (Lugol's solution) 10 m., water to 1 dr.

B.—Tincture of chloroform and morphine 5 m., tincture of catechu 15 m., syrup 20 m., mucilage of acacia 8½ m., water to 1 di.

[P1] **Ammonii Fluoridum.** In white deliquescent crystals which attack glass slowly. Has been used for the same purposes as the sodium salt. For phthisis, inhalation from a 1 in 500 solution has been recommended.

[P2] **Potassii Fluoridum** occurs in deliquescent cubic crystals or as a crystalline powder. It attacks glass slowly.

**Quininæ Hydrofluoridum.**  $\text{C}_{20}\text{H}_{24}\text{O}_2\text{N}_2\cdot\text{HF} = 344.2$

**Dose.**—1 to 2 grains (0.06 to 0.12 g). In relieving enlarged spleen and in rickets, also in exophthalmic goitre.

[P2] **Sodii Silicofluoridum (B.P.C.).** *Syn.* SODIUM FLUOSILICATE.  $\text{Na}_2\text{SiF}_6 = 188.1$ .

Fine white granular or crystalline powder, becoming gelatinous when moist. **Soluble** about 1 in 200 of water, giving a turbid acid solution. The 1 in 500 solution is non-caustic and has been used as an antiseptic. Concentrated solutions attack metal and porcelain enamel.

Two fatal cases of poisoning. Sodium silicofluoride is commonly sold as an insect powder. Half a spoonful, taken in mistake for carbonate, caused death in 10 hours. Hydrofluorsilicic acid is used as sterilising agent for pipes, etc., in breweries — *Chem Zeit*, 1925, 805, per *Analyst*, 1926, 313.

## ACIDUM HYDROCYANICUM

HCN = 27.02.

[P1] “Hydrocyanic acid; cyanides; double cyanides of mercury and zinc.”

[S1] “Hydrocyanic acid except substances containing less than 0.1% of hydrocyanic acid (HCN), cyanides except substances containing less than the equivalent of 0.1%, weight in weight, of hydrocyanic acid (HCN); double cyanides of mercury and zinc.”

[S6] “Hydrocyanic acid, cyanides; double cyanides of mercury and zinc”—specify proportion in a preparation as the proportion of hydrocyanic acid (HCN) that the preparation would be calculated to contain on the assumption that the cyanides in the poison had been wholly converted into hydrocyanic acid.”

Rule 20(2). “It shall not be lawful to sell or supply any compressed hydrocyanic acid unless the container is labelled with the words ‘Warning. This container holds poisonous gas and should only be opened and used by persons having expert knowledge of the precautions to be taken in its use’” (Note this rule is additional to other rules which apply to hydrocyanic acid and other poisons generally.)

[P1 S1] **Acidum Hydrocyanicum Fortius (B.P.C.)** *Syn.* SCHEEL’S HYDROCYANIC (or PRUSSIC) ACID.

**Dose.**—1 to 3 minims (0.06 to 0.2 ml.).

Manufactured by distillation of potassium ferrocyanide with dilute sulphuric acid.

A colourless liquid with powerful odour. Sp. gr. about 0.994. Contains approximately 4% HCN.

**Antidotes.** Give emetic immediately (may not be effective). Empty stomach by stomach tube, using 60 gr. of potassium permanganate in 2 gallons of water. Give, as chemical antidote, 15 gr. of ferrous sulphate, 20 m. of solution of ferric chloride and 1 to 2 dr. of magnesium carbonate mixed with a wineglassful of water; repeat this dose as required. Hydrogen peroxide, diluted about 1 in 16, may also be used. Artificial respiration, kept up steadily (20 per minute), oxygen, or oxygen and carbon dioxide

(7%) inhalations. Ammonia inhalations. Stimulants, *e.g.*, strychnine,  $\frac{1}{4}$  gr., or caffeine sodium benzoate, 2 gr., hypodermically. Intravenous injection of sodium thiosulphate, 10 to 50 ml. of 20% solution, or methylene blue, 50 ml. of 1% solution

#### References to Cyanide Poisoning and Treatment.

Review of cases of cyanide poisoning, antidotes most satisfactory seem to be sodium nitrite and sodium thiosulphate intravenously, and amyl nitrite by inhalation.—Chen, Rose and Clowes, *J. Amer. pharm. Ass.*, 1935, 625

80% of recoveries from 14 to 16 times the lethal dose of potassium cyanide given to rabbits by combined intravenous injections of sodium hyposulphite and inhalation of amyl nitrite —Per *Brit. med. J.*, 1/1934, 64.

50 to 70 ml. of a 20% sodium thiosulphate solution intravenously should be tried. A case where life was saved —*Brit. med. J.*, 1/1925, 1158.

Two intravenous injections of sodium thiosulphate, using 10 ml. of a 30% solution, of use in a case of potassium cyanide poisoning —*Prescriber*, 1927, 256

Potassium cyanide solution injected in lethal doses into guinea-pigs followed by glutathione shows that glutathione prevents death, especially when injected at the moment the guinea-pig falls into a coma. Acts apparently by stimulating renewal of tissue respiration —Regnier, *J. Pharm. Chim.*, 1934, 20, 501

Hydrocyanic acid used in industry, gilding, dyeing, fumigation, etc., it has been stated that no man should be without protection unless concentration of gas is less than 0.01%, and for long exposures concentration should be much lower than this

In ridding a house of bed-bugs it cannot be too strongly emphasised that fumigation by hydrogen cyanide is a dangerous process and should be undertaken only by responsible persons with full knowledge of the nature and properties of the gas, and who are skilled in the use of gas masks and oxygen breathing apparatus. In order to minimise risk, a lachrymating gas may be mixed with hydrogen cyanide to act as an indicator. Failure to detect the lachrymating gas, however, can of itself be accepted neither as indicating the absence of hydrogen cyanide nor that ventilation is complete —*Rep. med. Offr. Minist. Hlth. Lond.*, 1934, 161

Poisoning of a laboratory assistant who inhaled fumes from HCN lying in a concentrated sludge in a sink which escaped on stirring —*Brit. med. J.*, 1/1930, 132.

Hydrocyanic acid poisoning. Effects of being gassed —J. R. Graham, *ibid.*, 262.

Hydrocyanic acid for killing rats in ships no serious risk to foodstuffs —G. W. Monier Williams, *Brit. med. J.*, 1/1931, 65

[P1 81] **Acidum Hydrocyanicum Dilutum** (B.P., *P. Ned. V.*, *P. Belg.* IV, *Fr. Cx.*) *Syn* DILUTE PRUSSIC ACID

*Dose.*—2 to 5 minims (0.12 to 0.3 ml.) *Fr. Cx.*—Max. single dose  $1\frac{1}{2}$  minims, max. during 24 hours 8 minims

Contains 2% w/w of HCN, sp. gr. about 0.997. Keep in inverted stoppered bottles in the dark

*For the estimation of hydrocyanic acid and detection of minute amounts in toxicological work, see Vol. II*

**Incompatible** with soluble salts of silver, mercury and iron

**Uses.** In dyspepsia with pain, combined with bismuth or sodium bicarbonate. To allay vomiting and cough. It is very useful as a sedative in an effervescent mixture.

To promote healing of acute gastric ulcer bismuth, according to some, is of no particular value, but dilute hydrocyanic acid 5 minims in 2 drachms of water is useful for vomiting

[P1] **Lotio Acidi Hydrocyanici et Bicarbonatis** (L.H., *R. L. O. H.*)

Diluted hydrocyanic acid 5 m., borax 4 gr., sodium bicarbonate 4 gr., sterilised water to 1 oz. A soothing eye lotion.

[P1 81] **Potassii Cyanidum** (B.P.C., Fr. Cx.). *Syn* POTASSIUM CYANURET (an old name), KALIUM CYANATUM, CYANKALI, CYANURE DE POTASSE KCN = 65.10.

*Dose*.— $\frac{1}{2}$  to  $\frac{1}{4}$  grain (0.005 to 0.016 g.).

*Fr Cx* has *max single dose*  $\frac{1}{6}$  grain, *max* during 24 hours  $\frac{1}{2}$  grain.

A crystallised salt or in fused masses, deliquescent and decomposed on exposure to air.

**Soluble** 1 in  $2\frac{1}{2}$  of water, 1 in 10 of alcohol 90%

**Antidotes.** See Acid Hydrocyanic.

**TRADE VARIETIES** Commercial fused potassium cyanide is obtainable in various strengths, equivalent to 30, 40, and 90 to 95% of KCN; is also obtainable as a mixture with sodium cyanide (*gold cyanide*) containing the equivalent of 98 to 100% of KCN. 30% pure is supplied in sticks; this is "silver cyanide," for silver extraction. Sodium cyanide is equivalent to 130% of KCN.

**Potassium Cyanate**, KCNO, is made by oxidising potassium cyanide with red lead. Colourless crystals readily soluble in water.

**Potassii Ferricyanidum.**  $K_3Fe(CN)_6$  = 329.2. Red crystals. Used as a reagent and in photography.

**Potassii Ferrocyanidum.**  $K_4Fe(CN)_6 \cdot 3H_2O$  = 422.3. In lemon-yellow crystals.

*Dose*—8 grains (0.5 g.) Said to be physiologically almost without action.

**Potassii Thiocyanas.** *Syn* POTASSIUM SULPHOCYANIDE, POTASSIUM RHODANIDE KSCN = 97.2

*Dose*— $\frac{1}{4}$  to  $\frac{3}{4}$  grains (0.05 to 0.2 g.).

Made by fusing potassium cyanide with sulphur.

**Uses.** Has been employed as antispasmodic and anodyne—in phthisical cough and catarrh, dyspnoea, and mania. Mainly used in hypertension, treatment may begin with  $1\frac{1}{2}$  gr. three times a day and the dose decreased, or increased, up to 15 gr. per day, as required. Thiocyanates do not split off hydrocyanic acid and are not poisonous.

There is no clear evidence as to its clinical value in essential hypertension, and its hypotensive effect is almost always accompanied by distressing side reactions (weakness, fatigue, drowsiness, and gastro-intestinal symptoms) whether given in large doses for short periods or small doses for long periods. Arteriosclerosis a contraindication—D Ayman, *J Amer med Ass*, 1/1931, 1857. Both sodium and potassium thiocyanates produced very disagreeable side-effects—W C Egloff and co-workers, *ibid*, 1942.

Exfoliative dermatitis following use of  $1\frac{1}{2}$  grains three times daily for a week—C R Weis, *J Amer med Ass*, 11/1929, 988. Acute diffused erythematous dermatitis caused—*Brit med J Epit*, 11/1929, 96.

**Sodii Thiocyanas.** *Syn* SODIUM RHODANIDE, SODIUM SULPHOCYANIDE. NaCNS = 81.1

*Dose*.—1 to 5 grains (0.06 to 0.3 g.), up to 15 grains (1 g.) daily.

A crystalline colourless salt, soluble in water 1 in 0.3 and 1 in 0.6 of alcohol 90%.

**Uses.** It has a sedative action on the nervous system, is an analgesic, and may be found useful in nervous affections, arteriosclerosis, and chronic nephritis.

Favourable effect on pains of tabetics and in angiospastic



migraine has been reported. Is effective in reducing arterial hypertension.

The dose usually recommended is 2½ gr. twice or thrice daily after meals in an aromatic mixture. Up to 15 gr. daily tolerated over a period of three weeks.

The toxic and therapeutic effects of thiocyanates are often very close together and there are few indications that they are in any way superior, or even equal, to the older vasodilators — *Lancet*, ii/1932, 1169

Forty-five patients with hypertension were given sodium or potassium thiocyanate and the concentration of the cyanates in their blood followed. The reduction of blood pressure and the relief of symptoms obtained in thirty-five roughly corresponded to the level of the cyanates in the blood. The optimum therapeutic level would seem to range between 8 and 12 mg per 100 ml, and significant toxicity begins to appear at from 15 to 30 mg. The individual tolerance varies greatly, the different levels being obtained with widely varying doses. The cyanates may reach hazardous concentrations very quickly in some individuals, so that the administration of the thiocyanates is believed to be dangerous unless controlled by close observation and blood cyanate determinations — M H Barker, *J. Amer. med. Ass.*, 1/1936, 766.

**Rhodan-Calcotheobromine** (*Richter, London*). Calcium thiocyanate 0.1 g., theobromine-calcium 0.4 g. Dose — 1 or 2 tablets thrice daily. Nervous exhaustion, hypertension, arteriosclerosis

**Rhodocoffin** (*Richter, London*). Caffeine 0.11 g., sodium thiocyanate 0.04 g. Dose — 1 or 2 tablets daily. Exhaustion, headache

**Rhodopurin** (*Homburg Pharma Ltd, London*). Caffeine-thiocyanammonia in 5-grain tablets. Arterial hypertension

[P1 81] **Laurocerasus** (B.P.C.). *Syn.* CHERRY-LAUREL. The leaves of *Prunus Laurocerasus* (Rosaceæ).

[P1 81] **Aqua Laurocerasi** (B.P.C., *Fr. Cx.*, *P.G. V*, *P. Helv. V*).

Dose. — ½ to 2 drachms (2 to 8 ml.) Standardised to 0.1% of HCN. *P. Helv. V* requires this to be dispensed when Aqua Amygdalæ is prescribed.

## ACIDUM HYPOPHOSPHOROSUM

B.P.C., U.S.P. XI.

$H_3PO_4 = 66.0$ .

Dose. — 2 to 5 minims (0.12 to 0.3 ml.) U.S.P. XI average dose 3 minims.

A monobasic acid occurring as a colourless liquid containing 30 to 32% w/w of  $H_3PO_4$ . Sp. gr. about 1.14

**Antidotes.** Give copper sulphate as emetic, or use the stomach tube with dilute solution of potassium permanganate.

**Acidum Hypophosphorosum Dilutum** (B.P.).

*Syn.* ACIDUM HYPOPHOSPHOROSUM (*FE VIII*)

Dose. — 5 to 15 minims (0.3 to 1 ml.)

Contains 10% w/w of  $H_3PO_4$ . It may be prepared by diluting 323 g. of the B.P.C. concentrated acid with 677 g. of water (approximately 5 fl. oz. 440 m to 1 pint).

**Uses of Hypophosphites.** There is no reliable evidence that the hypophosphites exert any physiological effect. They are stated to be excreted unchanged in the urine, and any benefit may be

ascribed to the base with which the acid is combined. Hypophosphites are prescribed as a nervine tonic in anæmia and neurasthenia and also in disturbed nutrition and wasting diseases. In phthisis they may be given in full dosage for at least 6 months.

**Ammonii Hypophosphis.**  $\text{NH}_4 \text{H}_2\text{PO}_2 = 83.07$

*Dose*—1 to 6 grains (0.06 to 0.4 g.)

In white deliquescent tabular crystals, soluble 5 in 6 of water. Insoluble in alcohol. It has a nauseous saline taste. **Incompatible** with oxidising agents

**Calcii Hypophosphis** (*B.P.C.*, *P. Helv. V*, *P. Dan.*).

$\text{Ca}(\text{H}_2\text{PO}_2)_2 = 170.2$

*Dose*—3 to 10 grains (0.2 to 0.6 g.).

White crystalline salt, with nauseous taste, soluble 1 in 8 of water, insoluble in alcohol 90%. Prepared by heating phosphorus with milk of lime until phosphoretted hydrogen ceases to be given off, then filter and evaporate to crystallise or precipitate with alcohol.

**Incompatible** with oxidising agents

**Mistura Calcii Hypophosphitis.**

Calcium hypophosphite 5 grains, saccharated lime solution 1 drachm, peppermint water to 1 ounce

**Syrupus Calcii Hypophosphitis** (*B.P.C.*).

*Dose*.—1 to 4 drachms (4 to 16 ml.). Contains 1 grain per drachm

**Ferri Hypophosphis** (*B.P.C.*)  $\text{Fe}(\text{H}_2\text{PO}_2)_3 = 250.9$ .

*Syn.* FERRIC HYPOPHOSPHITE.

*Dose*.—1 to 3 grains (0.06 to 0.2 g.) in a pill or cachet.

Whitish amorphous powder with a chalybeate taste, and containing about 22% of Fe. Slightly **soluble** in water, but more so in presence of potassium citrate, or of hypophosphorous acid

**Liquor Ferri Hypophosphitis** (*B.P.C.*).

*Syn.* LIQUOR FERRI HYPOPHOSPHITIS FORTIS.

*Dose*.—10 to 30 minims (0.6 to 2 ml.)

[P. 81] **Pilula Ferri Hypophosphitis cum Strychnina** Strychnine  $\frac{1}{3}$  gr., ferric hypophosphite 2 gr. To make one pill (or in grammes to make 15)

*Dose*—1 twice or thrice daily

**Syrupus Ferri Hypophosphitis** (*B.P.C.*)

*Dose*— $\frac{1}{2}$  to 2 drachms (2 to 8 ml.)

Solution of iron hypophosphite 1, syrup to 5.

**Magnesii Hypophosphis** (*B.P.C.*).

$\text{Mg}(\text{H}_2\text{PO}_2)_2 \cdot 6\text{H}_2\text{O} = 262.5$

*Dose*.—3 to 10 grains (0.2 to 0.6 g.) White crystalline salt **soluble** about 1 in 5 of water

**Potassii Hypophosphis** (*B.P.C.*).  $\text{KH}_2\text{PO}_2 = 104.1$

*Dose*.—3 to 10 grains (0.2 to 0.6 g.)

A deliquescent granular white powder, having a nauseous, bitter taste. **Soluble** 1 in 0.6 of water, 1 in  $7\frac{1}{2}$  of alcohol 90%

**Incompatible** as the calcium salt

**Sodii Hypophosphis** (*B.P.C.*).  $\text{NaH}_2\text{PO}_2 = 88.03$  (+ $\text{H}_2\text{O}$ )  
*P. Ned. V*; about 1  $\text{H}_2\text{O}$  *P. Helv. V* and *P. Dan.*

**Dose.**—3 to 10 grains (0·2 to 0·6 g.).

A white granular deliquescent salt, with a bitter, nauseous taste.

**Soluble** 1 in 1 of water, and freely soluble in alcohol. Explosive when mixed with nitrates or other oxidising agents

**Fosfoxyl** (*Anglo-French Drug Co., London*) Sodium salt of hypophosphomonoterebinic acid, obtained by the combination of phosphorus and turpentine. Supplied as syrup or pills. **Dose**—One teaspoonful of syrup, or 2 pills, three or four times daily. In neurasthenia, anæmia, etc.

**Extractum Malti cum Hypophosphitibus** (*B.P.C.*).

Liquid extract of malt with  $\frac{1}{4}$  gr each of sodium and calcium hypophosphites per dr

[P1] **Glycerinum Hypophosphitum Compositum** (*B.P.C.*)

*Syn* GLYCEROL HYPOPHOSPHITIS

**Dose.**—1 to 2 drachms (4 to 8 ml.)

Contains the hypophosphites of calcium, potassium, manganese and quinine with about  $\frac{1}{80}$  gr of strychnine per dr. It is free from sugar.

[P1] **Syrupus Hypophosphitum Compositus** (*B.P.C.*)

*Syn.* SYRUPUS FERRI HYPOPHOSPHITIS COMPOSITUS

**Dose.**—1 to 2 drachms (4 to 8 ml.).

Contains the hypophosphites of calcium, potassium, manganese, and quinine with about  $\frac{1}{160}$  gr. of strychnine per dr

[P1] **Tabellæ Hypophosphitum Compositæ** (*B.P.C.*) are each equivalent to 1 drachm of the compound syrup.

## ACIDUM LACTICUM

*B.P., U.S.P. XI, P. Dan., P. Helv. V, etc*

$\text{CH}_3 \cdot \text{CHOH} \cdot \text{COOH} = 90\cdot05$

**Dose.**—5 to 20 minims (0·3 to 1·2 ml.), well diluted.

A colourless, odourless, syrupy, sour liquid, obtained by the fermentation of milk sugar by the action of *Bacillus acidilactici*. Lime or zinc oxide is used to neutralise the acid as formed. The respective lactates are then decomposed. It has sp. gr about 1·21 and consists of a mixture of hydrogen lactate and lactide ( $\text{C}_6\text{H}_8\text{O}_4$ ) containing the equivalent of not less than 87·5% of  $\text{C}_3\text{H}_5\text{O}_3$

*Fr. Cx* has sp. gr. 1·24 at 15°

**Solubility.** Is miscible with water, alcohol and ether; it coagulates milk and albumin

**Antidotes.** Empty stomach by stomach tube, using lime water. Give doses of magnesia stirred up in water (or chalk or magnesium carbonate, if magnesia is not available). Demulcent drinks.

**Uses.** It has been used locally in tuberculous ulceration of the pharynx and larynx, in diphtheria, etc., and internally for infantile and tropical diarrhoea, dyspepsia, to allay cough in phthisis, as a stomachic tonic in combination with iron and

alcium, and in vesical catarrh. A 1 in 10 solution is used as a douche in leucorrhœa. As a paint, or paste with kaolin, or as a 0% injection, it has been used in lupus, but is painful.

It is a constituent of some contraceptive pessaries and jellies. The secretion of the vagina is acid owing to the presence of about 0.5% of lactic acid which is secreted by Döderlein's bacillus. The motility of sperms is destroyed at pH 4 to pH 6, but in the act of coitus alkaline secretion is passed by the mucous membrane for the purpose of neutralising the acid. Lactic acid is therefore employed with the object of overcoming this alkalinity. Its effect is, however, largely neutralised by the buffering effect of seminal protein.

**Lactic Acid Milk** consists of fresh milk to which lactic acid 1 r. has been added drop by drop to each pint of milk. It is used for infant feeding and in gastro-enteritis.

**Hydrochloric Acid Milk** is made similarly, using 40 m. of dilute hydrochloric acid. It is used in lactalbumin sensitisation, specially for the eczema and asthma of children.

CHRONIC ENTERITIS treated with lactic acid  $7\frac{1}{2}$  minim doses *t d s p c*, the rationale being that *B. coli*, which is, as a rule, universally active in those cases where the motions are unduly offensive, cannot grow in a concentration of lactic acid of more than 1% — I H Lloyd-Williams, *Brit med J.*, 1/1923, 053.

TUBERCULOSIS OF THE LARYNX, in strengths of 50% and 100% in ulcerative cases.

### **Acidum Lacticum Dilutum (B.P.C.).**

*Dose.*— $\frac{1}{2}$  to 2 drachms (2 to 8 ml.).

Lactic acid 174.5 g., distilled water to 1000 g. (approximately fl. oz. to 1 pint). Contains about 16% *w/w* of  $C_3H_5O_3$ . Sp. gr about 1.04.

### **Injectio Acidi Lactici.**

Lactic acid 4 to 6 dr., water to 1 oz. In tuberculous ulceration has been injected into the tissues of the larynx.

Lactic acid injections used with benefit, particularly when the epiglottis is affected — R. Scott Stevenson, *Brit med J.*, 11/1933, 964.

### **Nebula Acidi Lactici.**

Lactic acid 1, distilled water 15. Of some use in diphtheria, appears to have the effect of dissolving the membranous exudation.

**Pessus Acidi Lactici (B.P.C.)** contain  $2\frac{1}{2}$  m. of acid in 30 gr. of oil of heobroma.

### **P2] Pigmentum Acidi Lactici cum Phenole (Mid H)**

Liquefied phenol 120 m., lactic acid to 1 oz. For lupus erythematosus.

### **Spiritus Acidi Lactici.**

Lactic acid 3, castor oil 2, lavender water 4, alcohol 90% to 24. Suitable for treatment of alopecia areata. To be rubbed in gently at first, later with some friction.

**Koromex** (Holland-Rantos Co., New York, Prentiss Ltd., London). Contraceptive jelly stated to contain boric, lactic and stearic acids and a stabiliser.

### **Syrupus Acidi Lactici (B.P.C.)**

*Dose.*—1 to 2 drachms (4 to 8 ml.).

Lactic acid  $2\frac{1}{2}$ % *v/v* in syrup.

### **Calcii Lactas (B.P., U.S.P. XI, P. Dan., P. Helv. V.).**

$(CH_3 \cdot CHOH \cdot COO)_2Ca \cdot 5H_2O = 308.2$

*Dose.*—15 to 60 grains (1 to 4 g.) Intravenously, 5 to 10 grains (0.3 to 0.6 g.) well diluted has been suggested. Subcutaneously too irritating. U.S.P. XI average dose is 15 grains.

**Solubility.** Samples vary in solubility, two kinds being obtainable. One has a solubility of 1 in 20 at 23°, and the other 1 in 16.—N. Glass, *Quart. J. Pharm.* 1933, 522.

The B.P. gives 1 in 18.5 (at 15°). The solubility does not decrease with age. Slightly soluble in alcohol

An opaque white crystalline powder.

**Uses.** Urticaria and chilblains have been treated with it. Chilblains are stated to be caused by a slow coagulation rate of the blood, which permits of effusion into the tissues and consequent swelling and inflammation. May be given in 15 gr. doses in chloroform water 1 oz., three times a day one hour before meals, to be continued over 6 weeks. Constipation, which is to be expected, may be corrected by a laxative. Prophylactically, 15 gr daily, e.g., three 5-grain tablets daily on an empty stomach for a week is useful to give prior to operation to increase coagulability of the blood, but is not always found suitable *per os*. Further, hypodermically, it has produced painful coagulation locally and collapse. Has been found of value in metrorrhagia. Is given during pregnancy (often in conjunction with vitamin D) to replace calcium taken by the foetus and to improve tone of involuntary muscle

MIGRAINE aborted by 30 gr of calcium lactate at first warning of onset — *Brit. med J Epit.*, 1/1926, 61.

#### **Liquor Calcii Lactatis (B.P.C.).**

**Dose.**—1 to 4 drachms (4 to 16 ml.) or more. Contains the equivalent of about 10 gr. of calcium lactate in 4 dr

#### **Mistura Calcii Lactatis (WH)**

Calcium lactate 15 gr, sodium lactate 5 gr., spirit of chloroform 5 m, water to ½ oz.

**Tabellæ Calcii Lactatis (B.P.C.)** contain 5 gr (0.3 g.)

#### **Tabellæ Parathyroidei et Calcii Lactatis (B.P.C.)**

**Dose.**—1 to 4 tablets.

Contain 5 gr. of calcium lactate and ¼ gr. of parathyroid.

**Calcii Lactas Recens.** The lactide does not interact unless the reactants are heated. A solution containing 100 gr. of calcium lactate is obtained by boiling for 20 minutes calcium carbonate 40 gr with lactic acid 1 dr. diluted with 10 dr of water, the diluted acid being added slowly to the carbonate. The product is filtered, the residue washed and the filtrate and washings diluted to volume.—*Pharm. J.*, 11/1930, 515

#### **Calcii et Sodii Lactas (B.P.C.).**

$\text{Ca}(\text{C}_3\text{H}_5\text{O}_3)_2 \cdot 2\text{NaC}_3\text{H}_5\text{O}_3 \cdot 4\text{H}_2\text{O} = 514.3.$

**Dose.**—5 to 30 grains (0.3 to 2 g.).

White powder or granules containing 8.5 to 9.5% of Ca, 10 to 11% of Na calculated on the dried substance, and not more than 16% of moisture.

Used for the same purposes as calcium lactate. The presence of sodium lactate is stated to increase the solubility and ease of absorption.

**Tabellæ Calcii et Sodii Lactatis (B.P.C.)** contain 7½ gr. (0.5 g.).

#### **Tabellæ Parathyroidei et Calcii et Sodii Lactatis (B.P.C.)**

**Dose.**—1 to 4 tablets.

Contain  $7\frac{1}{2}$  gr of calcium sodium lactate and  $\frac{1}{40}$  gr. of parathyroid

**Calsolact** (*Allen & Hanburys, London*) Tablets contain  $7\frac{1}{2}$  gr of calcium sodium lactate

**Kalzana Tablets** (*Wulffing, Berlin, Therapeutic Products, London*) are stated to contain  $3\frac{1}{2}$  gr each of calcium lactate and sodium lactate

**Nutritive Salts** (*Parke, Davis, London*). A combination of salts of calcium, magnesium, sodium, potassium, manganese, iron, etc., in 15 gr tablets For supplementing the diet in respect of mineral constituents, and preventing acidosis

### **Calcii Lactophosphas.**

*Dose.*—3 to 8 grains (0.2 to 0.5 g.)

Hygroscopic, crystalline powder. Some samples have consisted of a mixture of equal parts of calcium lactate and (dibasic) calcium phosphate **Soluble** in water Stomachic tonic In cardiac disease useful (Brunton)

**Liquor Calcis Lactophosphatis**, LACTOPHOSPHATE DE CALCIUM DISSOUS (*Fr. Cx.*)

Rub dibasic calcium phosphate 17, smoothly with water 964, add lactic acid 19 (*Fr. Cx.*, sp. gr. 1.24, practically pure acid)—all by weight Shake to dissolve, filter

### **Syrupus Calcii Lactophosphatis (B.P.C.).**

*Dose.*— $\frac{1}{2}$  to 1 drachm (2 to 4 ml.)

Contains the equivalent of 4 gr. calcium lactate per drachm

**Dusart's Syrup.** *Dose*—2 drachms to  $\frac{1}{2}$  ounce (8 to 15 ml.)

Calcium carbonate 9, lactic acid 75%, 22, phosphoric acid 10%, 88, water q.s. Dissolve the calcium carbonate in the lactic acid diluted to 108 with water with the aid of heat. Cool and add the phosphoric acid, and make up to 370. Dissolve in this sugar 623, and add spirit of limes 7. Mix and adjust to 1000. *All parts by weight*

### **Syrupus Calcii Lactophosphatis cum Ferro (B.P.C.).**

*Dose*— $\frac{1}{2}$  to 1 drachm (2 to 4 ml.)

Contains  $\frac{1}{2}$  gr. of ferrous lactate with potassium citrate and water in syrup of calcium lactophosphate to 1 dr

**Ferri Lactas** (*B.P.C., Fr. Cx., P. Belg. IV, P. Ital. V, P. Jap., P. Dan., P. Helv. V, Ph. Ned. V, F.E. VIII*). *Syn.* FERROUS LACTATE  $(C_3H_5O_3)_2Fe \cdot 3H_2O = 288.0$

*Dose.*—1 to 5 grains (0.06 to 0.3 g.).

In greenish white crystals with characteristic odour. **Soluble** 1 in 40 of water, readily soluble in alkali citrate solutions; when taken internally is easily assimilated by the system

**Magnesium Lactophosphas.** *Dose*—3 to 15 grains (0.3 to 1 g.), is a mixture of magnesium phosphate and magnesium lactate. A white powder soluble in water

**Potassii Lactas.**  $C_3H_5O_3K = 128.0$ .

*Dose*—5 to 15 grains (0.3 to 1 g.) Occurs as a syrupy liquid or as a very deliquescent amorphous mass soluble in water and alcohol 90%.

**Sodii Lactas.**  $C_3H_5O_3Na = 112.0$ .

*Dose*—5 to 10 grains (0.3 to 0.6 g.).

Usually in form of colourless or yellowish syrupy liquid miscible with water, containing 75% of the salt.

Large doses are said to be hypnotic. Is given intravenously as an isotonic ( $\frac{1}{8}$  molar) solution in all types of severe acidosis other

than that associated with congenital heart disease with persistent cyanosis, and for rapid alkalisation of the urine in the treatment of urinary infections.

The administration of sodium lactate prior to the use of chloroform has been suggested to prevent possible acidæmia. In other forms of acidosis the chief indication is when the  $\text{CO}_2$  content of the blood is below 25 vols per cent, when the dose should be 60 ml. per kg body weight. For alkalisation of urine, 30 ml per kg. body weight.

A concentrated (molar) stock may be made by neutralising 100 ml. of lactic acid with concentrated (about 40%) carbonate-free sodium hydroxide using phenol red as indicator, diluting to 800 ml. and boiling for 30 to 40 minutes, more alkali being added as necessary to neutralise the lactic acid produced by hydrolysis of lactide. The solution is diluted to 1000 ml., filtered and autoclaved at 15 to 20 lb. pressure for 30 minutes. For use this solution is diluted with five times its volume of sterile water.

**DIABETES MELITUS.** When there is tendency to acidosis, give sodium lactate or citrate in 40 grain doses, thrice daily.—Sir William Willcox. Three cases treated.—*Brit. med. J. Ept.*, 11/1921, 14.

**Lactate-Ringer Solution.** *Syn.* HARTMANN'S SOLUTION.

Add 10 ml. of concentrated (molar) sodium lactate solution to from 400 to 450 ml. of modified hypotonic Ringer's Solution (containing sodium chloride 6 g., potassium chloride 0.4 g., calcium chloride 0.2 g., magnesium chloride 0.2 g., water to 1000 ml.)

For all types of dehydration. Indicated especially for counteracting acidosis when sufficient sodium bicarbonate cannot be added to Ringer's Solution because of precipitation of calcium bicarbonate. *Dose*—80 to 100 ml per kg. body weight.

With 10% dextrose it is the fluid of choice for the continuous intravenous drip method.—A. F. Hartmann, *J. Amer. med. Ass.*, 11/1934, 1349.

**Physiological Buffer Solution (Hartmann Solution)** (*Lilly, London*)

*Dose*—For children up to one year 250 ml. of diluted solution, for children from 1 to 8, up to 1000 ml., subcutaneously, intraperitoneally or intravenously, in amounts sufficient to maintain elasticity of skin. Before using, the solution is diluted 25 times with freshly distilled water or glucose solution.

Not more than 30 ml. per kilo bodyweight is given. Indicated in dehydration with alkalosis or acidosis.

**Strontil Lactas** (*Fr. Cx*)  $(\text{C}_3\text{H}_5\text{O}_3)_2\text{Sr} \cdot 3\text{H}_2\text{O} = 319.8$ .

*Dose*—5 to 30 grains (0.3 to 2 g.)

A white crystalline powder, very soluble in water, of service in albuminuria and Bright's disease. May be combined with iron in the albuminuria of pregnancy. To increase coagulability of the blood 15 to 30 grain doses useful.

Tetany can be prevented or relieved by the continuous oral administration of strontium lactate. It acts by decreasing the permeability of the gut to calcium excretion and by reducing the excitability of the motor nerves.—*Brit. chem. Abstr.* (A), 1926, 318.

**Zinci Lactas.**  $(\text{C}_3\text{H}_5\text{O}_3)_2\text{Zn} \cdot 3\text{H}_2\text{O} = 297.5$

*Dose*.— $\frac{1}{2}$  to 3 grains (0.03 to 0.2 g.) *Max. pro die* 10 grains (Has been used in France up to 3 g. for a dose—Dorvault.)

White crystals soluble 1 in 60 of water. In epilepsy

## ACIDI LACTICI BACILLI

The salient points of Prof. Metchnikoff's well-known Lactic Acid Bacillus Therapy are given. *The subject is further dealt with in Vol. II.*

**Lactobacilline** (Darrasse, Nanterre, Wilcox, Jozeau, London), **Sauerin** (Allen & Hanburys, London), and **Trilactine** (Martindale, London) are commercial preparations of lactic acid bacilli. Liquid cultures are also on the market. These latter only remain active a month or less. *Moulded* tablets are said to show a higher initial count of the bacillus than compressed tablets.

The treatment, according to the severity and nature of the case, extends over one to three months. *Patient must avoid* foods such as gravy, meat jelly, meat extracts, white of egg, fat meat, high game, etc., which would act as culture-media for proteolytic bacilli.

**Lac Coactum (B P C.)—Curdled Milk.**

*Dose*—1 pint or more (less if not tolerated) *per diem*, divided into 2 or 3 portions.

After the bacilli have appeared in the stools, one daily dose, first thing in the morning or evening, is given. It is usually preferred during or after meals, but if taken on an empty stomach the organisms will pass through to the duodenum with less contamination with the stomach juices. Conduct the treatment for 3 weeks, then stop for a period before proceeding again. It should not be discontinued during the second week if flatulence is produced or constipation increased.

**Preparation of Curdled Milk.** The milk is sterilised by autoclaving at 125° for 30 minutes. It is cooled to 40° and placed in a suitable jar or basin so arranged with a small light beneath that a temperature of 40° to 45°C (104° to 113°F)—not higher—can be maintained for 8 to 10 hours. A ventilated dry heat (hot air) will work satisfactorily. For a pint of milk the requisite quantity of a liquid culture is added to the milk or two or more active lactic acid bacilli tablets—the quantity varies with the different brands—are crushed, *e.g.*, with a spoon, in a little of the previously heated and then cooled milk (reserved for the purpose), to make a paste and stirred into the remainder of the milk in the jar. For a quart four or more tablets should be employed. The milk will then (or a little later, *v. infra*) have formed a junket ready for consumption. If the curdled milk be “over made” (*i.e.*, much whey formed on the top), the heat must be reduced till the correct adjustment is ascertained.

Curdled milk may be taken, according to taste, either with sugar, or with cream and sugar, or with sugar and a little powdered cinnamon or ginger as flavouring. It is usually taken 12 to 24 hours after souring has been started. After 8 to 10 hours, *B. caucasicum* is in great preponderance in the cream—the bacilli appear to be carried up with the milk fat.

Acid production in milk begins immediately the milk is drawn from the cow, and in 48 hours sufficient acid (1%) is produced to coagulate the milk at normal temperature. For this reason dairy farmers have been known to add sodium bicarbonate, to counteract acidity and act as preservative. Some medical men think sodium lactate to be provocative of diarrhœa, and object to the addition.



**Uses.** Both the tablets and curdled milk are used for summer diarrhœa in children, diarrhœa and constipation in adults, skin affections, such as eczema and psoriasis, acne and furunculosis, infective disorders of the intestinal tract, such as typhoid, dysentery, for intestinal tuberculosis and tuberculous diarrhœa, and for cancer of the stomach or intestines, and in enteritis and colitis generally. Also as a cholagogue in hepatic congestion and gallstones, and in threatened appendicitis. May be of use in migraine, neurasthenia, and loss of appetite. The milk acts as a lubricant to the digestive tract, forming a pleasant article of diet, and may be taken in comparative health, as a nutrient and antiputrefactive.

**Contraindications.**—In some cases, notably in chronic acid gastritis, the stomach will not tolerate curdled milk. Many cases of enteritis are aggravated by milk in any form. Personal idiosyncrasy also enters into consideration. Suitable cases, those in which there is abnormal putrefaction of protein. Unsuitable, where symptoms are due to carbohydrate fermentation.—G. Herschell.

The bacterial flora of the intestine in health and chronic disease.—J. Cruickshank, *Brit. med. J.*, 11/1928, 555

**CHRONIC ENTERITIS** in infants. Lactic acid milk, soured biologically, has high curative value, and is possibly of value in infantile eczema and severe urticaria, but use of soured milk in the average home fraught with danger from pathogenic contaminations.—E. Cassie and U. Cox, *Lancet*, 11/1926, 325

**Local Use of Lactic-Ferment Preparations.**—A fresh culture of lactic acid organisms has been used to free the urethra from bacteria, e.g., in gonorrhœal infections. An ounce injected night and morning for a week resulted in lactic organisms only being found.

**Vaginal Suppositories of Lactic Acid Bacillus.**—A hard gelatin capsule (No. 11) is filled with liquid glucose—one daily for gonorrhœa. Upon decomposition of the glucose, acid is formed in which the large Bacillus Doderlein—a normal inhabitant—can grow. The acid kills off the pathogenic bacteria.—P. H. Marsden, *Pharm. J.*, 1/1920, 365

Cystitis has been treated by irrigation of the bladder with *B. bulgaricus*.

Vulvitis treated by smearing a paste of Bulgarian soured milk all over the vulva introducing if necessary a tampon soaked in it into the vagina. Combine this with gonococcal vaccine.—T. J. Abraham, *Clin. J.*, Feb., 1923, 73

**Lactochol** (Continental Laboratories, London). Lactic ferments, depigmented biliary extracts. Tablets and granules for intestinal affections.

**St. Ivel Lactic Milk** employing either *B. bulgaricus* or *B. acidophilus* is issued in card containers sufficient for a week's use, two cupfuls *pro die*.

**St. Ivel Lactic Cheese** is stated to contain 1.55% phosphate calculated as phosphoric acid, of which about 68% is in organic combination. *B. bulgaricus* is also present, and the number of organisms which have been found approach the number existing in soured milk.

**B. Acidophilus.**—Cheplin and Rettger say Metchnikoff worked with this and not *B. bulgaricus*.—*Prescriber*, 1923, 408. It is a first cousin of *B. bulgaricus* and not easy to distinguish. Doubt as to any real value in the acidophilus therapy. *B. acidophilus* is a normal inhabitant of the human intestine. Large quantities of the milk have to be taken, e.g., 1 litre a day, together with 300 g. of lactose.—*Brit. med. J.*, 1/1926, 713

**OBSTINATE CONSTIPATION** relieved almost without exception by daily doses of milk containing cultures of *B. acidophilus*. Should be prepared in the laboratory.—*Lancet*, 11/1926, 341.

In sprue of benefit.—*J. trop. Med. (Hyg.)*, Jan. 15, 1927, 23

**Bacillus Acidophilus Blocks.**

**Dose.**—3 to 4 daily for 6 to 12 weeks.

Contain *B. acidophilus* in agar jelly covered by a chocolate coating. They have the advantage of small volume, are palatable and contain no laxative drugs.

**B.A.C. Powder** (*Evans, Sons, Lescher & Webb, Liverpool*) Equal parts of dried *B. acidophilus* and *B. bulgaricus* in a living state in tubes containing one dose To be taken in cold or slightly warmed milk or water, preferably at night.

**Buttermilk** contains protein 3, fat 0.5, sugar 4.8, water 91 per cent The ordinary lactic acid bacilli found in this are not so active or resistant as those contained in Bulgarian sour milk Milk in any form, however, in sufficiently large quantity tends to lessen internal putrefaction Erysipelas has been cured by buttermilk internally and locally

**Buttermilk Powder (G.L.)** (*Glaxo Laboratories, London*) is milk from which greater part of fat is removed and some lactose has fermented Contains lactose 42%, protein 33.5%, fat 3.5%, lactic acid 6.5%, water 3.5%, etc. When reconstituted it gives a solution of pH 5 and acts as a buffered "acid-sparer," for use in the diarrhoeal diseases of infants.

**Ghee.**—A constituent of Indian dietary made by inoculating freshly-boiled milk (usually buffalo) with soured milk, and after curdling, skimming off the fat and heating in earthen pots Practically devoid of vitamin A—A. L. Bacharach, *Brit med J.*, 11/1930, 141

## ACIDUM NITRICUM

$\text{HNO}_3 = 63.02$ .

[P2] "*Nitric acid.*"

[83] "*Nitric acid—in substances containing less than 9%, weight in weight, of nitric acid ( $\text{HNO}_3$ ).*"

*Dose.*—1 to 4 minims (0.06 to 0.25 ml.).

B.P. has sp. gr. about 1.42, contains 70% w/w of  $\text{HNO}_3$ . U.S.P. XI, 67 to 70%, P. *Helv* V, 64 to 66%, P. *Ned* V, 50%; P.G. VI, 25%; Fr. Cx., and F.E. VIII, 63.64%; P. *Belg* IV, 63.02%; P. *Ital* V, 65.3%; P. *Dan.*, 22 to 25%.

**Antidotes.** Treat as for poisoning by glacial acetic acid, see p. 7 Chloroform in 5-drop doses every 10 minutes will prevent the convulsions following the inhalation of nitrous fumes, as in the accidental breaking of a bottle of nitric acid

**Uses.** A caustic for warts and condylomata

[P2] **Acidum Nitricum Dilutum** (B.P.C., Fr. Cx., F.E. VIII)

*Dose* —5 to 20 minims (0.3 to 1.2 ml.).

Contains 10% w/w of  $\text{HNO}_3$ . P. *Belg* IV has 12.6%.

Tonic and biliary stimulant

**Incompatible** with alkalis, sulphides, thiosulphates, ferrous salts, and alcohol.

[P2] **Acidum Nitricum Fumans.** Sp. gr. 1.5. (P. *Jap.* 1.486 to 1.5, P. *G.* VI has 86%, sp. gr. at least 1.476, P. *Dan.* has sp. gr. 1.48 to 1.5.)

A reddish-brown liquid, giving off yellowish-red fumes. Used as a caustic.

[P2] **Aqua Regia** is nitric acid 3, hydrochloric acid 4.

[P2] **Acidum Nitro-Hydrochloricum Dilutum** (B.P.C.).

*Dose.*—5 to 20 minims (0.3 to 1.2 ml.)

Contains nitric acid, hydrochloric acid and their reaction products equivalent to about 12.5% w/w of nitric acid and about 13.5% w/w of hydrochloric acid.

**Balneum Acidum** (B.P.C.). Contains 15 oz of dilute nitrohydrochloric acid per 30 gallons.

**Potassii Nitras** (B.P., U.S.P. XI, P. Helv. V, P. Dan.)

$\text{KNO}_3 = 101.1$ . Syn. NITRE, SALTPETRE

Dose—5 to 15 grains (0.3 to 1 g) Should be given well diluted. U.S.P. XI average dose 5 grains.

**Antidotes.** Empty stomach by emetic or stomach tube. Keep patient lying down and warm. Demulcent drinks freely. Stimulants, e.g., brandy,  $\frac{1}{2}$  oz in water, or hot coffee by mouth or by rectum.

**Uses.** Diuretic, to be given in dilute solution with caution. Its chief use is in the preparation of powders for burning in asthma. It has been found of value in chronic pericarditis in conjunction with other diuretics, and also in pneumonia in doses of 1 dr in solution every three hours for the first day, with gradual reduction on succeeding days.

Diuresis from potassium nitrate may be initiated more slowly and be of longer duration than that of other diuretics but it is less likely to cause untoward effects. It does not increase urinary acidity. It is best used in the form of enteric-coated pills of 0.5 g, of which 16 to 24 are given daily after meals. Patients are put on a salt-free, low-fluid diet and usually 50 g of protein daily, unless the serum protein is low, when it is increased to 75 or 100 g daily—N. M. Keith and M. W. Binger, *J. Amer. med. Ass.*, 11/1935, 1584.

Potassium nitrate in moderate dosage can be given for long periods of time without injury. A thirteen year old boy, weighing 110 pounds (49.9 kg), with glomerulonephritis took 6 g a day for a whole year, and thereby his œdema was kept under control. Intermittent administration is, however, to be preferred—S. Amberg, *Proc. Mayo Clin.*, 1935, 739.

**Charta Nitrata** (B.P.C., P. Dan.) Syn. NITRATED PAPER

White blotting-paper, impregnated with 20% potassium nitrate solution and dried. To relieve asthma these are burnt and the fumes inhaled.

Asthmatic pastilles are prepared in cones containing a mixture of chlorate and nitrate of potassium.

**Sodii Nitras** (P. Helv. V)  $\text{NaNO}_3 = 85.01$ .

Dose—5 to 15 grains (0.3 to 1 g.)

Has saline, refrigerant and diuretic properties.

**Uranii Nitras** (B.P.C.). Syn. URANYL NITRATE, URANIC NITRATE.  $\text{UO}_2(\text{NO}_3)_2 \cdot 6\text{H}_2\text{O} = 502.2$

Dose.—1 to 5 grains (0.06 to 0.3 g.) Lemon yellow radioactive crystals with bitter styptic taste, efflorescent in dry air.

**Soluble** 2 in 1 of water, also in alcohol and ether. Has been used in diabetes and cancer.

## ACIDUM OLEICUM

B.P., U.S.P. XI, P. Jap., P. Helv. V.

$\text{CH}_3(\text{CH}_2)_7\text{CH} : \text{CH}(\text{CH}_2)_7\text{COOH} = 282.3$ .

Dose.—5 to 15 minims (0.3 to 1 ml.).

A pale sherry-coloured, faintly acid, oily liquid (at ordinary temperatures) with a slight odour. **Soluble** readily in alcohol.

90%, ether, chloroform, benzene and fixed oils; insoluble in water. It dissolves most metallic oxides, thus forming indefinite solutions of oleates in an excess of oleic acid; such combinations of bismuth, copper, lead, mercury and zinc are used medicinally; they are soluble in fats. Oleic acid also dissolves alkaloids, but not their salts, *e.g.*, oleinates of aconitine, atropine ( $2\frac{1}{2}\%$  perfumed with otto), morphine and veratrine are used medicinally. Oleic acid is much more readily absorbed by the skin than oils

**Capsules of Oleic Acid**,  $7\frac{1}{2}$  minims *Dose*.—One or two daily

These are given for hepatic colic, and to hinder the formation of gall-stones. Best taken in the morning on an empty stomach

[**D P 1 81**] **Oleanodyne** (*Martindale, London*).

A special preparation combining the alkaloids aconitine, atropine, morphine (0.3%), and veratrine, with oleic acid. It is rapidly absorbed, and forms a strong anodyne liniment, which can be diluted with chloroform, alcohol, or oils

**To Prepare Metallic Oleates**.—Caspari recommends the preparation of (a) sodium oleate and (b) potassium oleate solutions in place of ordinary soap solutions (a) Warm 1217 gr. of oleic acid to  $60^{\circ}$  and add slowly 192 gr. of sodium hydroxide (90%) dissolved in a mixture of 2 oz. of distilled water and 6 dr. of alcohol, stirring constantly until acid neutralised (use phenolphthalein). Dissolve finally in 3 pints of water and filter (b) Neutralise 410 gr. potassium bicarbonate with 1156 gr. oleic acid in 1 pint of water by boiling. When cold make up to 3 pints. To the solution (a) add lead acetate (crystallised) 819 gr., copper sulphate 540 gr., zinc sulphate 621 gr., mercuric nitrate 711 gr., or to (b) lead acetate (crystallised) 777 gr., copper sulphate 510 gr., zinc sulphate 591 gr., or mercuric nitrate 675 gr., each dissolved in  $1\frac{1}{2}$  pints of water to produce the corresponding pure oleates

### **Bismuthi Oleas.**

*Dose* —5 to 10 grains (0.3 to 0.6 g.)

Dissolve bismuth nitrate (cryst.) 960 gr. in glycerin, 40 oz. by weight, in the cold. Add to the solution 3 pints of the above sodium oleate solution, wash by decanting, collect and dry. A greyish-white unctuous substance or white powder containing the equivalent of 20 to 22% of  $\text{Bi}_2\text{O}_3$ .

**Unguentum Bismuthi Oleatis** (*B.P.C.*)  $12\frac{1}{2}\%$  in white soft paraffin. For chapped hands and similar conditions

**Cupri Oleas** (*B.P.C.*).  $(\text{C}_{17}\text{H}_{33}\text{COO})_2\text{Cu} = 626$  1. (Theoretical formula for pure oleate).

Add a hot solution of copper sulphate 1 in 50 of water to a hot solution of castile soap 2.5 in 50, and wash and dry the precipitate. When cold it is in solid dark-green masses. It is an oleo-palmitate of copper, containing copper equivalent to about 12% of cupric oxide. Soluble in ether.

### **Unguentum Cupri Oleatis** (*B.P.C.*).

Copper oleate  $12\frac{1}{2}\%$  in yellow soft paraffin. For some purposes it may be employed half strength.

Ringworm is well treated with it—lightly rubbed in night and morning, also indolent ulcers, warts and corns, and it has been used to remove freckles.

**Bougies of Copper Oleate** are prepared 4 inches long containing each 5 grains (0.3 g.) of copper oleate with theobroma basis.

**[P2 81] Hydrargyrum Oleatum (B.P.).**

Yellow mercuric oxide 20% *w/w*, triturated with liquid paraffin and warmed with oleic acid Oleatum Hydrargyri, (*U.S.P. XI*) is made with 25% of HgO

**[P2 81] Unguentum Hydrargyri Oleati (B.P.).** *Syn* MERCURIC OLEATE OINTMENT.

Oleated mercury, 25%, in simple ointment

**[D P1 81] Oleatum Hydrargyri (10%) cum Morphina.**

Morphine (base) 1 is dissolved in 60 of the 10% oleate

**Uses.** For use where the plain oleate causes pain, in syphilis in secondary and tertiary stages, excessive use to be avoided. In persistent inflammation, especially of glands and joints (such as synovitis), and in non-ulcerated syphiloderma, these oleates are more active and cleanly than mercurial ointment They are very effective parasitocides for pediculi and ringworm

In rheumatoid arthritis the joints thickened by fibrous adhesions and fibroid thickenings of the synovial and periarticular tissues are treated with mercuric oleate

**[P2 81] Oleatum Hydrargyri cum Sulphure.**

Mercuric oleate 5% 4, precipitated sulphur 1, ether 3

For pediculi pubis.

**[P2 81] Unguentum Hydrargyri Oleatis Compositum.**—BROOKE'S OINTMENT—Mercuric oleate ointment (5%) and Lassar's paste of each 41, salicylic acid 6, ichthammol 12.

In (septic) œdema of the face has been applied covered with cotton wool in thick layer and pressed down by cotton elastic bandage.

**[P1 81] Emplastrum Hydrargyri Stearatis.**

Lead plaster 6, melt and add mercuric stearate 2, made by direct combination of mercuric oxide 10, with stearic acid 26 or *q s*—melt the acid and gradually stir in the oxide until all dissolved—a sand bath may be necessary Is a substitute for mercurial plaster

**[P2 81] Capsule of Mercuric Oleate Ointment** (*Martindale, London*) are soft capsules containing 30 gr. of the *B.P.* ointment**[P1 81] Plumbi Oleas (B.P.C.)**

An unctuous granular powder obtained by interaction of solutions of lead acetate and sodium oleate (*vide supra*).

**[P1 81 83] Emplastrum Plumbi (B.P.).** *Syn.* DIACHYLON PLASTER, DIACHYLON.

Lead plaster is a crude oleate of lead, made by the combination of olive oil (oleate and palmitate of glyceryl) and oxide of lead heated together in the presence of water. Thus made, the oleate is more adhesive than when prepared by the oleic acid solution of the oxide.

This has been used as an abortifacient

**Antidotes.** Treat as for poisoning by lead compounds, *see* p. 789

**[P1 81 83] Emplastrum Colophonii (B.P.).** *Syn.* EMPLASTRUM RESINÆ, ADHESIVE PLASTER.

Colophony 10, plaster of lead 85, hard soap 5

**[P1 81 83] Emplastrum Saponis (B.P.C.)** contains hard soap, colophony and plaster of lead. Is less adhesive than plaster of colophony.**Emplastrum Adhæsivum (U.S.P. XI)**

A rubber adhesive plaster prepared with 1.5 g. of a plaster mass, consisting of rubber, resins and waxes with a filler such as zinc oxide, orris root, or starch, on 100 sq. cm. of cotton cloth.

**Adhesive Plaster.**—Taffeta Adesivo (*P Ital V*)

Dissolve fish glue 100 g in small pieces in warm water 2000 ml, and add alcohol 95% 81½ ml and honey 10 g. Keep warm on a water-bath and apply 4 or 5 layers to fine silk tissue (allowing each layer to dry separately). Then apply balsam of Peru 1 g mixed with tincture of benzoin 4 g, and a final coating of glue. Dry, and keep away from air and light.

*P Helv V* has lead plaster 80, elemi 5, yellow beeswax 5, colophony 5, Venice turpentine (from *Larix decidua*) 5.

Local reaction to adhesive plasters occurs with considerable frequency. The following enter into the composition of adhesive plaster—(1) Rubber, one of more of four varieties South American Para, Plantation Smoked Sheet, Balata, Gutta siac (2) Rosin, Grade I (3) "Burgundy" pitch (4) Olibanum (5) Beeswax (6) Zinc Oxide (7) Anhydrous lanolin (8) Starch (9) Orris root. In patch tests carried out with 11 substances on 120 employees in a plaster factory, 21 showed degrees of reaction varying from slight erythema to erythema with oedema, papules and vesicle formation—*L. Schwartz and S M Peck, Publ Hlth Rep, Wash, 1935, 811*.

[**Pl 81**] **Unguentum Plumbi Oleatis** (*B P C*) *Syn* UNGUENTUM DIACHYLON, HEBRA'S OINTMENT. Plaster of lead 50% and olive oil, with 1% of oil of lavender.

[**Pl 81**] **Unguentum Diachyli Carbolisatum** (*Lassar*) is the same with 2% of phenol. To be rubbed in 1 to 3 times a day, or spread on linen and applied as a plaster.

These ointments are prescribed for eczema, excessive perspiration of the feet, etc.

**Zinci Oleas.**

Zinc sulphate 30 is dissolved in 60 of water, the solution is added to a solution of hard soap 90 in water 600, the mixture boiled and the zinc oleate washed, dried and powdered.

**Unguentum Zinci Oleatis** (*B P*)

Freshly-precipitated zinc oleate 1, white soft paraffin 1. Melt together and stir till cold. For some cases further dilution with soft paraffin is advisable. This ointment will cure chronic eczema.

**Zinci Oleostearas** (*B P C*)

A white amorphous powder with faint fatty odour.

**Manufacture.** To a solution of hard soap 2, and curd soap 1 in water 15, add zinc sulphate 1 in boiling water 2; wash free from sulphate, dry and powder.

Useful for dusting on eczematous surfaces and for excessive perspiration. It may be perfumed by the addition of 7.00 of thymol, and diluted with kaolin or starch.

**Pulvis Zinci Oleostearatis Compositus** (*B P C*) Zinc oleostearate 25, boric acid 25, starch to 100, perfumed with oil of geranium.

**Acidum Stearicum** (*B P C.*, *U S P. XI*, *P Jap.*, *P. Dan*, *P Helv V*) *Syn*. STEARINUM (*P. Austr.*) *Commercial Syn* "STEARINE," wrongly so called.  $C_{17}H_{35}COOH = 284.3$ .

This monobasic acid occurs as a hard white solid substance, and is not entirely pure. It is prepared by decomposition with superheated steam of stearin (the triglyceride of stearic acid contained with those of palmitic and oleic acids in tallow), and consists chiefly

of stearic and palmitic acid. **Soluble** about 1 in 18 of alcohol 90%, readily soluble in ether and chloroform.

M p. not below 54°.

It is obtainable commercially with m p. 50° (122°F.), 52.5° (126°F.), and 56° (132.8°F.) The pure acid melts at 69.2°.

**Pasta Acidi Stearici (B.P.C.)** *Syn* UNSCENTED VANISHING CREAM.

A non-greasy preparation containing partially saponified stearic acid Suitable for the application of substances such as quinine for the prevention of sunburn in artificial sunlight therapy

**Zinci Stearas (B.P., U.S.P. XI).**

A white powder, yielding 13 to 15.5% of ZnO Contains a small proportion of palmitate Manufactured by precipitating a curd soap solution with zinc sulphate

**Oleum Coccois (B.P.C.).** *Syn.* COCONUT OIL or BUTTER, OLEUM COCOS RAFFINATUM (*P. Dan*) Is obtained by expression from the kernels of the coconut, the fruit of *Cocos nucifera* and *C. butyracea* Becomes rancid on exposure to the air Forms a readily-absorbed ointment base. Is used commercially in the preparation of "marine" soaps

**Coconut Stearine.**—A solid fat separated from oil of coconut by cold pressure, m p. about 29° Has been suggested for use as a suppository basis

**Copra** is the dried pulp of the coconut.

The endocarp or meat of the nut is said to be a powerful tænicide The patient should drink the milk and then eat the endocarp.

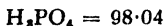
**Coconut Oil Soap.** This can be prepared by a simple cold process, not requiring anything in the nature of boiling To the fat, previously warmed to about 35°, an accurately measured quantity of caustic soda sp. gr. 1.35 (*i.e.*, 32%) is added with stirring (Use approx. 2½ of this lye to 5 of oil This will saponify with slight heating) The mass is allowed to stand and becomes warm, and saponification is effected in 24 hours The soap is not "salted out," that is, it contains the glycerin formed

**Liquor Saponis Olei Coccois (B.P.C.).** A solution of the sodium and potassium soaps of coconut oil, used as a shampoo and in dermatological practice.

**Unguentum Olei Coccois (B.P.C.)** 70% of coconut oil with white soft paraffin.

## ACIDUM PHOSPHORICUM

*B.P.*



*Syn.* ACIDUM PHOSPHORICUM CONCENTRATUM; CONCENTRATED PHOSPHORIC ACID.

Contains 89% *w/w* of  $\text{H}_3\text{PO}_4$ ; sp. gr. about 1.75. This acid is considerably stronger than the concentrated phosphoric acid of the *B.P.* '14, which contained 66.3% *w/w* of  $\text{H}_3\text{PO}_4$ , the sp. gr. being 1.5. *U.S.P. XI* has 85 to 88% of  $\text{H}_3\text{PO}_4$ ; *Fr. Cx.* and *P. Ital.* have 50%, sp. gr. 1.349; *P.G. VI* and *P. Ned. V* have 25%.

**Dose.**—1 to 4 minims (0.06 to 0.25 ml.).

**Antidotes.** Treat as for poisoning by glacial acetic acid, *see* p. 7.

**Acidum Phosphoricum Dilutum** (*B.P.*, *U.S.P. XI*, *P. Helv. V*, *P. Belg. IV*).

**Dose.**—5 to 20 minims (0.3 to 1.2 ml.).

Contains 10% of  $H_3PO_4$ , sp. gr. 1.054 to 1.060 *P. Dan.* has 12.2%, sp. gr. 1.067 to 1.07

Dilute concentrated phosphoric acid (89%) 112 g with distilled water *q s* to 1000 g An acid of approximately the same strength is obtained by diluting 1 fl oz 170 m of the concentrated acid with distilled water *q s* to 1 pint

**Incompatible** with alkalis, ferric chloride, lime salts

**Uses.** A nerve tonic and hæmatinic Said to increase the proportion of phosphates in the red blood corpuscles, and to increase the coagulability of the blood Well diluted, is a pleasant cooling drink in fevers, and relieves thirst in diabetes It renders iron preparations compatible with astringent vegetable infusions.

**Mistura Acidi Phosphorici** (*B.P.C.*).

**Dose** — $\frac{1}{2}$  to 1 ounce (15 to 30 ml).

Dilute phosphoric acid 15 m, with spirit of chloroform, syrup of orange and compound infusion of gentian to 1 oz

[**P1**] **Mist. Phosph. c. Strych.** (*N.I.F.*)

Dilute phosphoric acid 10 m, solution of strychnine hydrochloride 4 m, concentrated infusion of quassia 7½ m, water to ½ oz

**Fortossan** (*Ciba, London*) A combination of Phytin with lactose, specially suitable for infants and young children

**Phytin** (*Ciba, London*) Calcium magnesium salt of inositol hexaphosphoric acid with a phosphoric content of 22.8% **Dose**—One tablet 4 times daily, granules, 2 teaspoonfuls daily, powder, 4 gr 4 times daily Neurasthenia, tuberculosis, anæmia, etc

[**P1 81**] **Sympacrinol** (*Laboratoire de Sympathérapie, Neuilly-sur-Seine, Phargene Ltd., London*) Dragées contain Phytin 1.543 gr, boldo extract 0.154 gr, podophyllin 0.0463 gr., eserine salicylate 0.00077 gr, strychnine arsenate 0.00385 gr **Dose**—1 to 6 dragées daily Overwork, neurasthenia, convalescence, etc

**Ammonii Phosphas.**

**Dose**—5 to 20 grains (0.3 to 1.2 g)

A mixture of ammonium hydrogen phosphate,  $(NH_4)_2HPO_4 = 132.1$ , and ammonium dihydrogen phosphate,  $NH_4H_2PO_4 = 116.2$ , occurring in colourless crystals liberating ammonia on exposure to air.

**Soluble** 1 in 2 of water. A diuretic; increases the acidity of the urine.

**Calcii Phosphas** (*B.P.*). *Syn.* CALCIUM PHOSPHORICUM TRIBASICUM (*P. Helv. V*), "NEUTRAL" or "TRIBASIC" CALCIUM PHOSPHATE, CALCIUM ORTHO-PHOSPHATE.  $Ca_3(PO_4)_2 = 310.25$ .

**Dose.**—10 to 30 grains (0.6 to 2 g.), but larger amounts (up to 75 gr) are given as antacid

It consists mainly of the tribasic and dibasic phosphates with some monobasic compound. The pure tribasic compound is not obtainable.

White powder made by interaction of calcium chloride with



sodium phosphate and excess of ammonia at a boiling temperature. Insoluble in water; soluble in dilute hydrochloric and nitric acids.

**Uses.** To supply calcium to growing bones and to assist in general nutrition. It is also given to pregnant women for the same purpose. Is a useful antacid, and has the advantage of not producing systemic alkalisation.

**GASTRIC ULCER.** Bismuth carbonate is not an alkali, sodium bicarbonate gives off carbon dioxide and causes distension and in excess stimulates gastric secretion. Best method of avoidance of free acid and mechanical irritation is by giving hourly feeds of 5 ounces of milk, or its equivalent, through a tube, and neutralising acid by giving doses of atropine  $\frac{2}{3}$  gr increased to tolerance. Sodium citrate prevents milk clotting. Manganese oxide, dose regulated to keep bowels open and tribasic calcium or magnesium phosphate (chiefly the former) *effectually prevents acidosis*. Stomach emptied last thing at night — A. F. Hurst, *Lancet*, 1/1930, 242.

**Calcii Phosphas Di-acidus** (*Fr. Cx*, *F.E. VIII*, *P. Belg. IV*, *P. Helv. V*). *Syn.* MONOBASIC CALCIUM PHOSPHATE, OR ACID CALCIUM PHOSPHATE.  $\text{Ca}(\text{H}_2\text{PO}_4)_2 \cdot 2\text{H}_2\text{O} = 270.2$  *P. Helv. V* has  $\text{H}_2\text{O}$ .

*Dose.*—5 to 20 grains (0.3 to 1.2 g.).

Deliquescent crystals, insoluble in alcohol.

Mix calcium mono-acid phosphate 154 g with phosphoric acid (50%) 200 g. to a paste, and leave to stand 1 hour at about 50°, add water sufficient to make clear, and boil  $\frac{1}{2}$  hour. Evaporate to sp. gr. 1.40 (taken on the warm liquor) and leave to crystallise — *Fr. Cx*.

**Calcii Phosphas Mono-acidus** (*Fr. Cx*, *P. Ned. V*, *F.E. VIII*, *P. Belg. IV*, *P. Ital. V*, *P. Helv. V*, *P. Dan.*) *Syn.* DIBASIC CALCIUM PHOSPHATE, CALCIUM MONO-HYDROGEN PHOSPHATE  $\text{CaHPO}_4 \cdot 2\text{H}_2\text{O} = 172.1$

*Dose*—10 to 30 grains (0.6 to 2 g.) Prepared by decomposing calcium chloride with dibasic sodium phosphate

Colourless crystals with slight acid reaction. Used in making *Liquor Calcis Lactophosphatis*, *q.v.*

**Dicalcium Phosphate Dulcet** (*Abbott, Montreal, Pharmaceutical Products, London*). A candy preparation of dicalcium phosphate, containing 24% calcium and 20% phosphorus. Each Dulcet contains 1 g. In calcium deficiency diseases.

**Potassii Phosphas** (*B.P.C.*). *Syn.* DI-POTASSIUM HYDROGEN PHOSPHATE.  $\text{K}_2\text{HPO}_4 = 174.2$ .

*Dose.*—10 to 30 grains (0.6 to 2 g.).

A deliquescent granular powder, is given as a saline purge.

**Potassii Phosphas Acidus.** *Syn.* POTASSIUM DI-HYDROGEN PHOSPHATE, MONO-POTASSIUM PHOSPHATE  $\text{KH}_2\text{PO}_4 = 136.1$ .

*Dose.*— $\frac{1}{4}$  to 1 drachm (1 to 4 g.).

Colourless crystals, readily soluble in water with acid reaction. Resembles the sodium compound, but is more diuretic.

**Sodii Phosphas** (*B.P.*, *P. Ital. V*, *F.E. VIII*). *Syn.* DI-SODIUM HYDROGEN PHOSPHATE; TASTELESS PURGING SALT.  $\text{Na}_2\text{HPO}_4 \cdot 12\text{H}_2\text{O} = 358.2$ . *P. Ned. V*, *P. Belg. IV* and *P. Helv. V* have  $2\text{H}_2\text{O}$ . *U.S.P. XI* and *P. Dan.* have  $7\text{H}_2\text{O}$ .

**Dose.**— $\frac{1}{2}$  to 4 drachms (2 to 16 g) *U.S.P. XI* average dose 1 drachm Colourless crystals, efflorescent in dry air.

**Soluble** 1 in 7 of water, almost insoluble in alcohol 90%.

A mild aperient, well suited for a delicate stomach, small doses are antacid and diuretic, useful in bilious sick-headache and jaundice.

For hepatic calculi, 60 grains 3 times a day, with  $\frac{1}{10}$  grain sodium arsenate added, is given if any evidence of gastro-intestinal catarrh.

### **Sodii Phosphas Exsiccatus** (*U.S.P. XI, P. Helv. V*)

$\text{Na}_2\text{HPO}_4 = 142.0$

**Dose**—10 to 75 grains (0.6 to 5 g.) A white powder, readily absorbing moisture

**Soluble** 1 in 15 of water.

### **Sodii Phosphas Effervescens** (*B.P.*)

**Dose.**—1 to 4 drachms (4 to 16 g).

Contains 50% of sodium phosphate. A convenient and pleasant mode of taking this useful purgative

### **Sodii Phosphas Effervescens** (*U.S.P. XI*)

**Average dose**—150 grains (10 g) Contains about 20% of exsiccated sodium phosphate with sodium bicarbonate, tartaric acid and citric acid

**Alka-Zane** (*Warner, London*)

**Dose**—1 teaspoonful in a glass of cold water 3 or 4 times daily after meals. An effervescent preparation of sodium, potassium, calcium and magnesium citrates, carbonates and phosphates. An antacid-diuretic, maintaining "alkali reserve"

**Calsoma** (*Abbott, Chicago, Pharmaceutical Products, London*) Granular effervescent preparation of calcium and magnesium tribasic phosphates, sodium bisphosphate and magnesium citrate, for acid indigestion

### **Sodii Phosphas Acidus** (*B.P., U.S.P. XI*)

*Syn.* SODIUM DIHYDROGEN PHOSPHATE, SODIUM BIPHOSPHATE,  $\text{NaH}_2\text{PO}_4 \cdot 2\text{H}_2\text{O} = 156.1$

**Dose.**— $\frac{1}{2}$  to 1 drachm (2 to 4 g) *U.S.P. XI* average dose 10 grains.

In colourless crystals or crystalline powder. **Soluble** about 1 in 1 of water, and 1 in 300 of alcohol 90% Is given in alkalinity of urine with good results. Particularly useful in cystitis, and after operations on the bladder to keep the urine acid. If diarrhoea occurs, stop its use for a time.

Passage of a calcium oxalate stone may be assisted by employing this salt owing to its solvent action on calcium oxalate. The salt given by the mouth is eliminated as such. 2 ounces *per diem* in 100 ounces of distilled water were administered, and in 6 weeks no symptoms of stone remained. The solvent action can be demonstrated *in vitro*. The treatment is advised in cases of calcium oxalate deposit without stone formation.

### **Mistura Sodii Phosphatis Acidii** (*L.H.*).

Sodium acid phosphate 30 gr., red mixture to  $\frac{1}{2}$  oz. (*Mistura Rubra L.H.* fuchsin  $\frac{1}{1000}$  grain, water  $\frac{1}{2}$  oz.).

### **Mistura Sodii Acid-Phosphatis Composita** (*L.H.*).

With each dose of the previous mixture, patient to take hexamine 5 gr.

**Mist. Sod. Phosph. Acid.** (*N I F.*)

Sodium acid phosphate 20 gr, liquid extract of hyoscyamus 4 m, concentrated infusion of buchu 7½ m, chloroform water to ½ oz.

**Phospho-Soda (Fleet)** (*C. B Fleet Co., Lynchburg, Va; Anglo-French Drug Co., London*). Monosodium phosphate in a non-toxic, highly concentrated aqueous solution. *Dose*.—As a laxative and liver stimulant, one teaspoonful before meals; as a purgative, 3 or 4 teaspoonfuls before breakfast, for hyperacidity due to constipation, 1 teaspoonful an hour after meals. Dilute with a third of a glass of water, and follow by a full glass.

**Recresal (Braun, London)** Tablets of sodium acid phosphate. *Dose* —2 to 5 daily. Muscular and nerve tonic.

**Sodii Phosphas Neutralis.** *Syn* TRIBASIC SODIUM PHOSPHATE, NORMAL SODIUM PHOSPHATE.  $\text{Na}_3\text{PO}_4 \cdot 12\text{H}_2\text{O} = 380.2$

Used for softening water and for boilers, preventing incrustation. Soluble in water with alkaline reaction, dissociation giving sodium hydrate.

**Sodii Pyrophosphas** (*P Ned IV, P. Helv. V, F E VIII*)

$\text{Na}_4\text{P}_2\text{O}_7 \cdot 10\text{H}_2\text{O} = 446.2$

*Dose*.—5 to 30 grains (0.3 to 2 g.).

Is obtainable by heating the orthophosphate,  $\text{Na}_2\text{HPO}_4 \cdot \text{H}_2\text{O}$ . White crystals readily soluble in water. Uses similar to those of the phosphate.

**Sodii Pyrophosphas Acidus**,  $\text{Na}_2\text{H}_2\text{P}_2\text{O}_7$ , is a white amorphous powder soluble in water. Is sometimes used in baking powder.

**Sodii et Ammonii Phosphas.** *Syn* MICROCOSMIC SALT

$\text{Na}(\text{NH}_4)\text{HPO}_4 \cdot 4\text{H}_2\text{O} = 209.1$  Used in chemical analysis with the blow-pipe and for estimation of magnesium.

## ACIDUM SALICYLICUM

*B P., U S P XI, P Helv V, P Dan., etc*

$\text{C}_6\text{H}_4(\text{OH})\text{COOH} = 138.05$

*Syn.* o-HYDROXYBENZOIC ACID.

*Dose* —5 to 10 grains (0.3 to 0.6 g.).

*Fr. Cx.* gives max. single dose 1 g; max during 24 hours 4 g.

Salicylic acid (artificial acid) of commerce is made by Kolbe's method devised in 1874, by heating sodium phenate in a current of carbon dioxide, or by a modification of it. The basic sodium salicylate so formed is decomposed with hydrochloric acid. A modification (R. Schmitt's) consists in heating the phenate and gas under pressure, this is more economical.

It may also be prepared from salicin and from oils of wintergreen (*Gaultheria procumbens*—Ericaceæ) and sweet birch (*Betula lenta*—Betulaceæ). This natural acid was formerly preferred for internal use.

In colourless prismatic crystals with sweetish taste. It is odourless, but its dust irritates the nostrils. *M.p.* 158° to 159°.

**Soluble** 1 in 500 of cold water, 1 in 35 of 90% alcohol, 1 in 40 of 45%, 1 in 2 of ether, about 1 in 80 of olive or almond oil, 1 in 100 of castor oil, 1 in 200 of glycerin, and 1 in 55 of chloroform; soluble also in melted fats and soft paraffin. Borax, ammonium citrate and sodium phosphate increase its solubility in water.

**Incompatibility.** Spirit of nitrous ether, quinine salts, alkalis such as sal volatile. An aqueous solution of the acid gives a deep violet colour with a trace of a ferric salt.

**Uses.** Anti-fermentative and anti-putrefactive For various febrile conditions, generally as one of its salts, particularly for acute rheumatism, *v.* Sodii Salicylas In stomatitis a saturated aqueous solution is used. Large doses alone act as a direct poison on the heart and affect respiration. It is applied to corns, warts and lupus.

A saturated aqueous solution as **Rectal Injection** has been used for dysentery of children.

To eradicate stumps left after removal of papillomatous growths 1 to 6% solutions in spirit. It may also be used dissolved with sodium sulphurinate, *q.v.*

For sweating feet Pulvis Salicylicus cum Talco is used.

A solution of 1 dr. of acid in 1½ oz. of methylated spirit has been used as a paint for ringworm of nails, with scraping every night, the applications being continued for 3 months or longer.

For SCARLATINAI SORE THROATS and tonsillitis, compresses of 2% alcoholic solution found of value. In gonorrhœa, may prove irritant, necessitating periodical dropping and renewal.

To remove TATTOO MARKS, mass salicylic acid with glycerin to a dough—apply over the marks with a compress and strips of adhesive plaster and allow to remain in contact for a week. After the first dressing the epidermis over the marks is removed and a fresh application of the salicylic paste applied. Usually the second application removes.

**Amylum Salicylatum (B.P.C.)** Salicylic acid 1, starch 9

**Collodium Salicylicum (B.P.C.)** About 1 in 8 in acetone and acetone collodion

[P1 §1] **Collodium Salicylicum Compositum (B.P.C.)** *Syn* COLLODIUM CALLOSUM

Salicylic acid about 1 in 8, and extract of cannabis, in acetone and acetone collodion.

**Collod. Callosum (N.I.F.)** Creosote 6 m, salicylic acid 27 gr, collodion to 2 dr

[P1 §1] **Collodium Callosum (St B.H.)** Salicylic acid 1 dr., zinc chloride 20 gr, extract of cannabis 10 gr, flexible collodion to 1 oz

**Collodium Salicylicum et Lacticum.** Salicylic and lactic acids of each 10, collodion 80. Lactic acid, being destructive of morbid growths, is said to increase its efficacy.

**Collyrium Acidi Salicylici (B.P.C.)** 0.1% *w/v.*

[P1 §1] **Emplastrum Salicylicum Compositum (B.P.C.).**

Salicylic acid 20% and extract of cannabis 10% in rubber adhesive plaster.

[P1 §1] **Emplastrum Salicylicum Compositum Fortius (B.P.C.).**

Salicylic acid 40% and extract of cannabis 20% in rubber adhesive plaster.

**Emplastrum Salicylicum Elasticum (B.P.C.).** 10% in rubber adhesive plaster. Plasters are also prepared with other proportions (from 5 to 40%) of salicylic acid.

WARTS often yield to prolonged maceration by a strong salicylic acid plaster—up to 60% strength—cut exactly to the pattern and outline of the lesion. The use of fuming nitric and other strong acids should be banished.—H. C. Semon, *Practitioner*, 11/1933, 479

**Liquor Acidi Salicylici.**

Boiling distilled water 1000 parts, salicylic acid  $1\frac{1}{2}$  parts. A good antiseptic gargle. A useful solvent for alkaloidal and other salts, it is irritating to the eyes.

**Oleum Acidi Salicylici.**

Scabs in eczema are well treated by salicylic acid dissolved in castor oil, 1 in 50. This dissolves on warming.

**Parogenum Salicylatum (B P C)** *Syn* SALICYLATED VASOLIMENT.

Salicylic acid 10% *w/v* in parogen

**Pulvis Acidi Salicylici Compositus (B P C)** *Syn* PULVIS PRO PEDIBUS

Salicylic acid 3% with boric acid and purified talc

**Pulvis Salicylicus cum Talco.**

Salicylic acid 3, wheat starch 10, talc 87

Mix to form a fine powder. For perspiration of the feet

**Pulvis Zinci et Acidi Salicylici (B P C)**

Zinc oxide 20% and salicylic acid 5% in starch

[P2] **Salicylic Cream or Paste.**

Salicylic acid, in powder, 2, phenol 1, glycerin 10, mix.

Used as pigment when the skin is irritated by the discharge from wounds, etc., under antiseptic dressings

**Salicylic Gauze, Lint and Wool, each 4%**

Dissolve the salicylic acid in alcohol, *q.s.* (about 1 = 1 of dressing) and impregnate under pressure. dry.

**Unguentum Acidi Salicylici (B P)**

Salicylic acid, in powder, 1, white paraffin ointment 49. Useful in eczema, acne and ringworm. A 50% ointment has been used in lupus vulgaris, scabies, acute eczematous dermatitis and ringworm.

In seborrhœa, the following is useful: salicylic acid 1, precipitated sulphur 2.5, cold cream 25.

**Adsorption through the Skin.**

Salicylic acid can be transported through the epidermis into the connective tissues and thence into the blood stream. The colloids of the connective tissues retain the drug by adsorption and from these surfaces it is liberated gradually, passes into the blood and is mainly excreted by the kidney. The excreted portion may be estimated colorimetrically in mg. per 100 ml. urine, and if the quantity of urine voided in the 24 hours is known the total urinary excretion of salicylic acid may be calculated. Adsorption may take place from soft paraffin, alcohol and water, but the first is probably the best.—H. Leslie-Roberts, *Brit. J. Dermat.*, Aug., 1928, 325

Dermatitis may in some instances be caused by the external use of salicylic acid and its derivatives.—*Yearb. Pharm.*, 1924, 341.

DUPUYTREN'S CONTRACTION. 5% salicylic acid ointment found effectual in several weeks.—D. A. Alexander, *Brit. med. J.*, i/1923, 794

[P2 81] **Mycozol (Parke, Davis, London).** Chlorethone 5%, salicylic acid 4%, and mercury salicylate 4%, in a suitable ointment base. For the treatment of fungus infections of the skin. Also Liquid Mycozol, a paint containing chlorethone, malachite green, salicylic acid, etc.

**Salicylosol** (*Pearson, Mitcham*) A solution of salicylic acid in a partly oxygenated mineral oil Used by massage into the skin

**Ammonii Salicylas** (*B.P.C., U.S.P. XI*).

$C_6H_4(OH) \cdot COONH_4 = 155.08$ . *P. Ned. V* with  $\frac{1}{2} H_2O$ .

**Dose.**—5 to 15 grains (0.3 to 1 g.), up to 30 grains (2 g.) is sometimes given *U.S.P. XI* average dose 15 grains.

In crystalline powder, soluble 1 in 1 of water, 1 in  $2\frac{1}{2}$  of alcohol 90%.

"Merely another salicylate," possessing no special advantages over sodium salicylate, or over other ammonium salts Can be dispensed with from the materia medica —C C Johnson and P J Hanzlik, *J Pharmacol*, July, 1929, 332

In large doses is liable to cause gastric disturbance

**Ferri Salicylas.** *Syn.* FERRIC SALICYLATE. Composition varies.

**Dose** —3 to 10 grains (0.2 to 0.6 g.).

Brownish powder, sparingly soluble in water, but readily in solution of potassium bicarbonate.

In tonsillitis, as an antiarthritic tonic, and as a dusting powder for foul wounds.

**Mistura Ferri Salicylatis** (*B.V.H.*).

Potassium bicarbonate 10 gr., sodium salicylate 10 gr., solution of ferric chloride 5 m., water to 1 oz. Useful in erysipelas and acute tonsillitis

**Mistura Ferri Salicylata.** COHEN'S SALICYLATED IRON MIXTURE

**Dose** —1 to 2 drachms (4 to 8 ml.) increased

Dissolve citric acid 14 in distilled water 200, add ammonium carbonate 6.5, then dissolve sodium salicylate 125 in this solution, add tincture of ferric chloride 125, glycerin 175, and oil of betula 4, and then add sufficient distilled water to make 1000, and filter

**Lithii Salicylas** (*B.P.C.*)  $C_6H_4(OH) COOLi = 144.0$ .

**Dose** —10 to 30 grains (0.6 to 2 g.)

A deliquescent white powder, **soluble** more than 1 in 1 of water, forming a colourless, slightly acid solution, 1 in 2 of alcohol 90%, and in ether.

**Incompatible** with acids and with sodium bicarbonate.

**Used** in rheumatism and gout Varicose veins have been treated with lithium salicylate and Tutocaine.

Lithium salicylate 30% with Tutocaine 1%, 5 ml injections into the larger veins and a similar amount of sodium chloride solution 20% with Tutocaine added, for smaller veins at weekly intervals until sclerosis is complete —P. M. Deville, *Brit med J*, 11/1930, 1000

Lithium salicylate 30% with Tutocaine 1%, 4 ml and quinine urethane 2 ml, injected simultaneously using two syringes, 3-4 in. apart. Quinine salicylate deposited —R H. Maingot, *Brit med J*, 1/1932, 1054

Lithium salicylate 30% with Tutocaine 0.75%, scleroses well and produces no symptoms. Sodium chloride 20% with Tutocaine 0.75% good for small veins, especially if thin-walled and the skin over them atrophic It should however, not be used in large healthy veins Quinine-urethane best from point of view of thrombosis but many do not tolerate it even in smallest doses "Twin injections" good, viz., 4 ml. lithium salicylate solution and 2 ml of quinine-urethane simultaneously, injections being 3 to 5 in. apart Only to be used if veins are very large. The lithium solution to be given first —N. Scott, *Brit med. J.*, 11/1930, 58.

**Effervescent Lithium Salicylate** contains 1 in 30.

**Dose.**—1 or 2 drachms.

**Magnesi Salicylas** (*B.P.C.*).

$(C_6H_4(OH) COO)_2Mg \cdot 4H_2O = 370.5$ .

**Dose.**—8 to 30 grains (0.5 to 2.0 g.).

In crystals or as a white or pinkish crystalline powder. **Soluble** 1 in 6 of water. Incompatible with acids and sodium bicarbonate. It has been given in typhoid.

In flatulence 15 to 45 grains thrice daily has been found useful

**Potassii Salicylas** (B.P.C.).  $C_6H_4(OH)COOK = 176.1$ .

**Dose.**—10 to 30 grains (0.6 to 2 g.)

A white crystalline powder, very soluble in water.

Has given relief in rheumatic affections of the eyes

**Sodii Salicylas** (B.P., U.S.P. XI, P. Helv. V, P. Dan.)  
 $C_6H_4(OH)COONa = 160.04$

**Dose.**—10 to 30 grains (0.6 to 2 g.) in a mixture or in cachets

**Fr. Cx**—*Max single dose*, 30 gr., max. during 24 hours, 180 gr. approximately; **F.E. VIII** 140 gr.

*Intravenously* doses as large as 15 grains (1 g.) have been given, also in combination with the same amount of sodium iodide (see *Injectio Sodii Salicylatis*)

In white scales or shining tabular crystals with sweetish taste

**Soluble** 1 in 1 of water, and 1 in 6 of alcohol 90%. Natural and synthetic varieties are available in commerce, the former being obtained from the natural acid. Concentrated aqueous solutions should be made with hot water and filtered, they are liable to deposit crystals of the hexahydrate on standing

**Storage.** *P. Belg IV* and *P. Helv V* direct to be kept in the dark.

**Incompatible** with free ammonia, ammonium carbonate, and aromatic spirit of ammonia (turns brown). Gives a violet colour with iron salts. Mineral and many organic acids and acid salts cause separation of salicylic acid, *e.g.*, to dispense sodium salicylate with tincture of ferric chloride, dissolve 1 dr. of the salt in 2 oz. of water, add 30 to 40 m. of the tincture and 1½ oz. of a solution of potassium bicarbonate 1 dr. in 1 oz., then chloroform water to 8 oz. The result is a clear, palatable, claret-coloured mixture useful in rheumatic sore throats combined with anæmia.

**Uses.** Rheumatism, neuralgia, diarrhoea (of young children, said to be almost specific), vertigo, Menière's disease, and diabetes may all be well treated by salicylates. In influenza and acute tonsillitis, 10 grains every 3 hours relieves the distressing symptoms. Puerperal fever, biliousness, acute pains of fibrositis, nephritis, cystitis, urticaria and Graves' disease have been well treated with it. It is considered the most powerful of hepatic stimulants. As a urinary antiseptic (*per os*) it has less action than hexamine—about 50% of that given is excreted as salicylic acid.

Sympathetic ophthalmia has been treated with large doses—1 gr. per pound body weight in divided doses during 10 to 14 hours.

The itching of pruritus ani may be instantly relieved by application of a very minute quantity of sodium salicylate.

In sciatica the electro-negative salicylic ions have been used by Iontophoresis.

In acute rheumatism some advise very large doses, *e.g.*, 150 gr. daily, with twice the amount of sodium bicarbonate or even *double* these amounts. Sodium bicarbonate should always accompany it to prevent toxic effects due to its action on the central nervous system

Rectal injections of 8 g. in 150 ml with 1.5 ml tincture of opium have been employed.

Intravenously, 1 g. doses have been given in rheumatic affections. The stimulation is more rapid than in doses *per os*. Injections are of great value in acute streptococcal arthritis but are less effective in so-called chronic arthritis, although more permanent results are obtained by using sodium iodide in addition. Injected into an inflamed rheumatic joint, the pain disappears and the patient can move the joint. For its use in the injection treatment of varicose veins, *vide infra*.

FATAL INTOXICATION in a child of 10 years treated for rheumatic endocarditis. After 5 days' salicylate treatment (2 g intravenously and 5 g rectally) symptoms of intoxication due to an acidoketosis of salicylate origin, together with renal insufficiency, developed, and despite intensive alkalinisation death occurred three days later. Post-mortem revealed discrete renal lesions and massive fatty degeneration of the liver.—G. Paiseau, *per Brit med J Epit*, ii/1934, 61.

#### References.

CHOREA believed to be always rheumatic, at least in part, therefore give sodium salicylate lest fresh rheumatic manifestations develop, which might thus be avoided. Smaller doses advocated than those of Lees (with sodium bicarbonate). Before starting treatment bowels should be freely opened, and before increasing dose evacuation should have taken place during preceding 12 hours. Chloretone as sedative sometimes useful in 3 to 5 grain doses—F Langmead. R Stockman does not believe in the salicylic treatment of chorea, but prefers arsenic and nerve sedatives.

ENCEPHALITIS LETHARGICA treated by sodium salicylate, 15 to 30 gr. every 4 hours. When there is insomnia give 5 to 10 gr of bromide and iodide of potassium—A G. Gullan, *Brit med J*, i/1925, 1120

RHEUMATIC FEVER. Relapses found to be common when the dose was reduced too rapidly or the treatment stopped. It might be considered reasonable to keep all cases of rheumatic fever, except the most trivial, on a daily dosage of 120 gr for a month after admission to hospital. The initial dose to be aimed at in an adult should be 200 to 240 gr daily, with double the quantity of sodium bicarbonate, continued until toxic signs develop or the temperature has been below 99°F. for 24 hours. Thereafter a reduction to 180 to 150 gr might be allowed for 10 days, and after that 120 gr until the end of the fourth week, continuing with daily doses of 60 gr. until the patient is ready to be allowed out of bed, when 30 to 45 gr of acetylsalicylic acid might be substituted for a time.—R. M. Murray-Lyon, *Edinb med J.*, Feb., 1936, 84

In acute and subacute rheumatism in children, sodium salicylate intramuscularly is of advantage, 1 gr for each year in 1 ml water once a day for 4 days. Temperature normal in 24 hours and pains gone—but does not control rheumatic cardiac disease. There is no specific drug for the cardiac infection, but cases benefit by digitalis—E C. Warner, *Lancet*, ii/1930, 719

For immediate treatment the salicylates are the most efficacious remedies at present known.—G. A. Allen, *Prescriber*, 1926, 400.

Salicylates appeared best in preventing subsequent carditis developing, next in order being arsenic, sedatives giving rest only—Mary Bertram, *Brit. med J*, i/1925, 496.

RHEUMATIC POLYARTHRITIS well treated by *large doses*, giving 10 times daily at 2-hourly intervals 50 ml of a solution containing sodium salicylate 30 g, sodium bicarbonate 60 g, syrup of orange 300 g, and distilled water to 1000 ml. When fever and pains have disappeared, reduce to 4-hourly intervals. Quick



cure in acute cases, and the accompanying endocarditis is improved or cured.—J. T. Peters, *J. Amer. med. Ass.*, 11/1929, 958.

#### References to Intravenous Use.

ENCEPHALITIS LETHARGICA well treated by sodium salicylate intravenously.—*Lancet*, 1/1924, 1011.

HÆMORRHOIDS treated by interstitial injection of 30% solution. Results as good as those obtained with phenol (*vide* Hamamelis) but the pain immediately after the injection is more severe and lasts longer—J. Dunbar, *Brit. med. J.*, 11/1923, 809.

PNEUMONIA. Injections of a 1 in 30 solution (dose not stated) intravenously efficacious in all pneumococcic pulmonary infections—per *J. Amer. med. Ass.*, 11/1929, 1078.

PSORIASIS. In selected difficult cases, intravenous injections (10 ml. of a 20% solution, three times weekly for 4 or 5 weeks) appear to be of definite value—*Brit. med. J. Epit.*, 1/1925, 26.

RHEUMATIC PAIN. Injected into an acutely inflamed rheumatic joint, the pain disappears and the patient is able to move his joint. This points to a specific action, since analgesia is central—Dixon, p. 255.

RHEUMATISM (ACUTE). Refractory cases treated by large doses intravenously—*Brit. med. J.*, 1/1931, 70.

"Opsonised salicylate" in rheumatic fever. Into a 20 ml. syringe first 5 to 8 ml. of 20% sodium salicylate solution, then 8 to 10 ml. of blood from patient's median basilic vein. After 4 minutes it is injected. Temperature dropped and patient better—*Lancet*, 1/1929, 245.

SCIATICA (ACUTE). Effect sometimes dramatic—better than *per os*—F. J. W. Porter, *Lancet*, 11/1925, 1306.

TYPHUS FEVER treated with encouraging results by sodium salicylate intravenously, injections, frequently up to 5 and 6 g., being given daily. Myocarditis a contraindication—*Jl. Intrav. Therap.*, Jan., 1926, 20.

### Varicose Veins.

Sodium salicylate in 20, 30 or 40% solution may be used as the sclerosing agent in the injection treatment of varicose veins, the dose being 6 to 10 ml. of the 20% at the first sitting, then 4 to 5 ml. of the 30% and finally 2 to 4 ml. of the 40%. The veins rapidly acquire a toleration for the drug if obliteration does not occur rapidly. The injection, especially of the 40% solution, may cause intense pain, commencing some seconds after injection and lasting for 2 to 3 minutes. Immediate pain on injection is an indication of extravasation of the sclerosing solution. Addition of  $\frac{1}{2}$ % of procaine hydrochloride has been advised, but may prevent recognition of extravasation of the solution.

There are several disadvantages, including possible loss of time in testing sensitivity of the patient, acquirement of tolerance by veins if they are not quickly obliterated, cramp during administration, ulceration if leakage occurs, uncontrollable effect—A. H. Douthwaite, "The Injection Treatment of Varicose Veins," H. K. Lewis, 1927.

V. Meisen recommends sodium salicylate 25%, and sodium chloride 10%, which is practically painless. *Max. dose*—10 ml. Cannula (not too sharp) is inserted with patient standing, rotate once or twice when blood flows from it to see that it has not caught in the opposite wall. The patient then lies down with leg on a special stand. When varices are empty commence injection very slowly, stopping if flow is resisted or if patient feels pain. For injections in the neighbourhood of the malleoli inject  $\frac{1}{2}$ % Novocaine direct into the varix. Massage lightly after injection. Repeat the treatment every other day and if both legs are affected treat one every day. Reference is also made to Sicard and L. Humbert—*Lancet*, 1/1927, 1355.

The standard injection now for a medium-sized vein is 5 ml. 30% solution in 10% saline, and for a large vein 7 ml. of 40% solution in 10% saline. Inject with limb emptied of blood and from below upwards. The effect can be judged

after a fortnight. Local analgesics added to allay the pain found entirely negative. —G H Colt, *Brit med J*, 11/1929, 850

25% saline with 5% salicylate is a good average "guidable" solution for those who prefer saline to salicylate —G H Colt, *Brit med J*, 1/1930, 760

Sclerosing agents used with safety for 6 years in Chile —S M Wells, *Lancet*, 1/1929, 951

Salicylates, 30 and 40%, intensely painful —Alan Perry, *Lancet*, 11/1929, 901

20% sodium salicylate causes no "salicylate cramp" —L P H Crivelli, *Brit med J*, 1/1930, 618.

**Relative Value of Sclerosing Solutions** Sodium salicylate painful and accompanied by cramps in the calves. Even a small quantity getting into the tissues is irritant. A large percentage do not "take" —D Levi, *Lancet*, 11/1930, 16

Sodium salicylate not so certain in its effects as quinine and invariably caused cramps —Reginald Payne *Brit med J*, 1/1932, 238

Poisoning following 4 intravenous injections of 5 ml 20% sodium salicylate solution for varicose veins —œdema, urticaria, nausea, and vomiting —*Brit med J Ept*, 1/1928, 31

**VARICOSE ULCERS** As the result of a questionnaire to 550 medical men, A. P. Luff concludes that the treatment is best limited to two procedures (1) Injection of veins (preferably with sodium salicylate) in combination with Unna's zinc gelatin for local treatment, (2) Unna's zinc gelatin alone if injection is refused or cannot be done. Ultra-violet light treatment appears very reliable in the hands of experts. The rational method of prevention of varicose ulcers is the obliteration of varicose veins. —*Brit med J*, 11/1928, 1146

See also *Glucose, Lithium Salicylate, Quinine-Urethane, Sodium Morrhuate, Sodium Chloride and Therapeutic Index.*

**Scleroveine** (Bengué, London) Sodium salicylate solution in ampoules for varicose vein injection

**Sterules of Sodium Salicylate** (Martindale, London) contain 15 gr in 320 m (1 g in 20 ml) Also available containing 1 g of sodium iodide for chronic arthritic affections

**Effervescent Sodium Salicylate.** This is made in two strengths—5 and 10 grains in a drachm

**Dose**—1 drachm (4 g) or more

**Mist. Sod. Sal. (N I F)**

Sodium salicylate 10 gr, sodium bicarbonate 15 gr, concentrated compound infusion of gentian 15 m, water to  $\frac{1}{2}$  oz.

[P1] **Mistura Coryzæ (B V H)**

Tincture of catechu 15 m, sodium salicylate 6 gr, ammonium chloride 5 gr, compound tincture of cinchona 1 dr, compound tincture of chloroform and morphine 5 m, syrup of tolu 30 m, syrup of lemon 30 m, glycerin 15 m, mucilage of acacia 15 m, liquid extract of nux vomica  $\frac{1}{2}$  m, water to 1 oz. Apparently a bad example of polypharmacy but if any ingredient be omitted it disagrees with some patients. As it stands it can be taken by everybody —A T Todd, *Practitioner*, 1934, 731

**Strontii Salicylas** ( $C_6H_4(OH)COO)_2Sr, 2H_2O$  - 397.7.

**Dose**—5 to 20 grains (0.3 to 1.2 g)

A white crystalline powder, slightly soluble in water and in alcohol

**Used** for chronic gout, and is a good intestinal antiseptic

**Intravenously** 10 ml of 5% solution, has proved useful in chronic affections of the joints. The lactate may be given orally, and, in severe pain, the bromide intravenously in place of the salicylate. —*Per Pharm J.*, 11/1926, 287.

**Methylis Salicylas** (B P., U.S.P. XI, P. *Helv.* V, P. *Dan.*)

$C_6H_4(OH) \cdot COOCH_3 = 152.1$ . **Syn** ARTIFICIAL (OR SYNTHETIC) OIL OF WINTERGREEN

**Dose** —5 to 15 minims (0.3 to 1 ml.). *U.S.P. XI* average dose 12 minims.

*U.S.P. XI* gives *Oleum Gaultheriæ* and *Oleum Betulæ* from the bark of *B. lenta* (Sweet Birch) as synonymous with methyl salicylate.

*P. Belg. IV* directs methyl salicylate to be given when *Essence de Wintergreen* is prescribed. *F.E. VIII*—May be either synthetic or natural. *P. Ital. V*—Synthetic only.

A colourless liquid, with wintergreen odour.

May be prepared by carefully distilling a mixture of salicylic acid 2, methyl alcohol 2 and sulphuric acid 1. **Miscible** with alcohol 90%, ether, chloroform or glacial acetic acid.

**Antidotes.** Empty stomach by emetic, or by using stomach tube with 4 oz. of sodium bicarbonate in 2 gallons of water. Give water freely, with sodium bicarbonate or magnesia, then milk and demulcent drinks. Keep patient lying down and warm.

**Poisoning** due to swallowing 1 oz. of methyl salicylate. Recovery after forcing liquids by the mouth, 2% solution of sodium bicarbonate by proctoclysis and wrapping patient with blankets —*J. Amer. med. Ass.*, 11/1925, 306

Less than 15 ml. *per os* has caused more than one fatality in infants. 13 cases of poisoning have been recorded, with 6 deaths —*Brit. med. J. Epit.*, 1/1928, 57

**Uses.** Is readily absorbed when applied to the skin, and is an efficient application in lumbago, sciatica and rheumatic pain, either alone as a paint, or as a liniment or ointment. Also used for furunculoid ulcers, orchitis and mumps.

### **Linimentum Methylis Salicylatis (B.P.C.)**

*Syn.* LINIMENTUM BETULÆ COMPOSITUM.

Rectified oil of camphor 1 in 4, with menthol, oil of eucalyptus and methyl salicylate.

### **[P1] Linimentum Methylis Salicylatis Compositum (B.P.C.)**

Rectified oil of camphor 1 in 4, with menthol, chloral hydrate, methyl salicylate and chlorophyll.

### **Linimentum Methylis Salicylatis Oleosum (B.P.C.)**

*Syn.* LINIMENTUM METHYLIS SALICYLATIS SIMPLEX

Methyl salicylate 25% *v/v* in rape oil.

### **Unguentum Methylis Salicylatis (B.P.C.)** *Syn.* UNGUENTUM METHYLIS SALICYLATIS FORTE.

Contains 50% *w/w* of methyl salicylate

### **Unguentum Methylis Salicylatis Dilutum (B.P.C.)**

Contains 25% of the strong ointment in hydrous wool fat ointment.

### **Unguentum Methylis Salicylatis Compositum (B.P.C.).** *Syn.* UNGUENTUM METHYLIS SALICYLATIS COMPOSITUM FORTE, UNGUENTUM BETULÆ COMPOSITUM, UNGUENTUM ANALGESICUM, ANALGESIC BALM.

Contains methyl salicylate 50% *w/w*, menthol 10% *w/w*, oil of cajuput and eucalyptol in a beeswax and wool fat basis.

### **Unguentum Methylis Salicylatis Compositum Dilutum (B.P.C.).**

Contains 25% of the strong compound ointment in hydrous wool fat ointment

**Analgesic Balm** (*Parke, Davis, London*) Menthol, methyl salicylate and lanolin. Muscular pain, rheumatism, etc.

**Balmosa** (*Oppenheimer, Son & Co, London*) A non-greasy, analgesic cream containing methyl salicylate and rubefacients

**Betul-Oil (Huxley Brand)** (*Anglo-American Pharmaceutical Co., Croydon*) See Vol II.

**Menthofax** (*Burroughs, Wellcome, London*). Contains methyl salicylate 50%, menthol 10%, eucalyptol 2.5%, oil of cajuput 2.5%, white beeswax 20% and hydrous wool fat 15%

**Mesotan** (*Bayer Products, London*) Methoxymethyl salicylate Used in the form of a paint, diluted with 1 to 4 parts of olive or other oil as a counter-irritant

**Methylsal Balm** (*Martindale, London*) Contains methyl salicylate 7, in combination with menthol 5%. Also prepared containing 25% and 33% of methyl salicylate (with menthol 5%) For analgesic effect in rheumatism

**Oleum Betulae.** Syn OIL OF SWEET BIRCH, OIL OF WINTER-GREEN, OLEUM GAULTHERIÆ

*Dose*—5 to 15 minims (0.3 to 1 ml.)

Formerly obtained from *Gaultheria procumbens*, now exclusively from *Betula lenta*. Contains not less than 98% w/w of esters, calculated as methyl salicylate

The oil has similar properties to salicylic acid 10 to 20 minims are given every 3 or 4 hours in rheumatism and sciatica With olive oil externally for rheumatism.

**Relpar Ampoules** (*Anglo-French Drug Co, London*) Natural salicylic acid in distilled *Betula lenta* water *Dose*—8 to 10 ml daily subcutaneously, but not more than 1 ml. at one locality. Rheumatism, sciatica, gout, etc

**Salicinum** (B.P., U S P XI.)

$C_6H_{11}O_6 \cdot O \cdot C_6H_4 \cdot CH_2OH = 286.1$

*Dose.*—5 to 15 grains (0.3 to 1 g) in cachets, tablets or in aqueous solution—the taste being covered with liquid extract of liquorice, or small doses may be given in a pill with glycerin of tragacanth.

A glucoside in colourless shining trimetric tabular crystals, without odour, taste moderately bitter Obtained from various species of *Salix* and *Populus* especially *S. fragilis*.

**Soluble** 1 in 28 parts of cold water, and 1 in 80 of alcohol, but insoluble in ether or chloroform.

**Uses.** Given for influenza and as a prophylactic. In rheumatic fever it is highly satisfactory. 20-grain doses hourly, or 30 grains every 2 or 3 hours. 60 grains have been given, repeated in 2 hours without ill effect. It is given to reduce fevers, e.g., of malaria or phthisis. Is of value in psoriasis, lupus erythematosus and in syphilis where mercury is not tolerated. It is not adapted for use as an external antiseptic.

Its value in influenza from 1889 to 1927.—E B. Turner, *Brit. med. J.*, ii/1927, 97, see also J. Craig, *ibid.*, 237.

**PSORIASIS.**—Salicin, 10 to 15 grains three times a day a valuable drug in acute and spreading cases.—B.M.A. Ann Meeting, 1926, *Lancet*, ii/1926, 550. See also G Pernet, *Arch Derm Syph N Y*, Jan., 1926, 111

**Effervescent Salicin.** Dose—1 drachm. Contains 5 grains in 1 drachm.

**Tabellæ Salicini** (B.P.C.) contain 5 gr (0.3 g.).

**Salol** (B.P.C., P. Belg. IV, P. Ital. V, F. E. VIII, U.S.P. XI, P. Helv. V, P. Dan.).

*Syn.* PHENYL SALICYLATE.  $C_6H_4(OH)COOC_6H_5 = 214.1$ .

*Dose.*—5 to 20 grains (0.3 to 1.2 g.) in cachets, suspended in milk, or in mixtures suspended with tragacanth *Fr. Cx.* and *P. Belg.*: *Max. single dose*, 15 gr.; *max. during 24 hours*, 90 gr. *P. Helv. V.* has *max. single dose* of 30 grains

Small crystals, with a slight wintergreen odour *M.p.*  $42^\circ$  to  $43.5^\circ$ .

**Soluble** 1 in 15 of alcohol 90%, 1 in 10 of liquid paraffin, in fixed oils, and a trace in glycerin. Almost insoluble in water.

**Dispensing Note.** When prescribed in an emulsion with an oil, *e.g.*, castor oil, dissolve it in the oil before proceeding. Melt the salol in the oil in a warmed mortar, emulsify with acacia, using hot water to complete

In the case of the following prescription, salol 10 gr., castor oil 5 m, tragacanth *q.s.*, glycerin 10 m and water to 1 oz., it is well to use saponin. Place the castor oil, salol and glycerin in a mortar with half a grain of saponin, triturate well together, then add gradually with continuous stirring  $\frac{1}{2}$  oz. of mucilage of tragacanth, and, finally, the requisite quantity of water. This method produces a fine, white, non-separating emulsion.

**Uses.** Antiseptic and antipyretic. In the small intestine it splits up into its component parts, both being found in the urine which becomes very dark. The phenol exerts a disinfectant action on the urinary tract. Used with success for rheumatism, acute and chronic, for sciatica, dysentery, typhoid fever, and gonorrhœa and vesical catarrh. Is used as an intestinal antiseptic, but effective doses would be toxic owing to liberation of phenol.

In all forms of sore throat, relieves earache and ocular neuralgia, and of value for summer diarrhœa, especially of children. Must not be given in renal disease.

**SALOL COATING OF PILLS** is conducted by employing salol *melted*. This renders the pill insoluble in the acid gastric juice, but soluble in the alkaline fluid of the intestine, hence suitable for purgatives to act on the bowels, and for administering antiseptics in eczema and urticaria—*cf.* *Pilulæ*

**Collodium Salol.** Salol 4, ether 4, collodion 30.

**Emulsio Salol.** *Dose*— $\frac{1}{2}$  to 1 ounce (15 to 30 ml.)

Salol 20 gr, compound tragacanth powder 20 gr, distilled water *q.s.* to 1 oz

**CHOLERA** During the algid stage the following mixtures have been used.—Salol 10 gr, mucilage 1 dr., spirit of chloroform 15 m, water 1 oz.—every 2 hours until reaction sets in—then sodium bicarbonate 10 gr, spirit of chloroform 20 m, spirit of nitrous ether 20 m, water to 2 dr every 4 hours till urinary secretion is established and normal. May be combined with 2 or 3 quart intravenous injections of warm sodium chloride solution (100 gr. to the quart). This injection is made by gravity (2 or 3 feet head of water), and may be repeated.—Brooke.

**Liquor Salolis Compositus** (B.P.C.). *Syn.* SALOL MOUTH WASH. Salol 2.5% with thymol, oil of peppermint, oil of anise, elixir of saccharin and alcohol 90%. For use, add  $\frac{1}{2}$  to 1 teaspoonful to a tumbler of water

**Pigmentum Salolis (B.P.C.).** Salol 1 in 300 in glycerin and alcohol 90%. For septic tonsils.

**Salol Catheter Oil.** Salol 1, castor oil and almond oil, of each 15 Does not dissolve the varnish of catheters.

**Salol cum Camphora.** *Syn* SALOL CAMPHOR

Salol 3, camphor 2, heated together, combine to form a viscid liquid, which has been used as an antiseptic in place of iodoform Prepared with 10% only of camphor, quickly crystallises, and when powdered is suitable for application where liquid is not practicable.

Useful in suppuration of the middle ear, non-irritating

**Tabellæ Salolis (B.P.C.)** contain 5 gr. (0.3 g.).

[D P1 81] **Unguentum Salol cum Cocaina.**

Salol 2, cocaine hydrochloride 1, ceratum petrolei 16. For burns

**Unguentum Salol cum Menthol.**

Salol 4, menthol 2, olive oil 4, wool fat to 100 For fissures of the skin, *e.g.*, in chapped hands

**SUNBURN.** A 10% cream made by dissolving the salol in a minimum amount of liquid paraffin and mixing this solution with a base of cold cream, makes an effective application for the absorption of ultra-violet rays and prevention of sunburn—H Sharlit, *Arch Derm Syph*, N Y, Aug, 1935, 291.

**Saliod (Gabail)** (*Anglo-French Drug Co., London*) Ampoules of 5 ml. contain 1 g of salol and 0.1 g of iodine, with 0.02 g of camphor, in ether-purified olive oil *Dose*—5 ml intramuscularly every 2 days Chronic rheumatism.

## OTHER ESTERS OF SALICYLIC ACID

**Amylis Salicylas.**  $C_6H_4(OH)COOC_2H_5 = 208.1$ .

Colourless liquid with carnation odour, used principally in perfumery Has been used for painting on rheumatic joints.

**Capsules of amyl salicylate** contain 3 minims (0.2 ml) for internal medication

**BURNS**, especially from acids, are well treated with a pad soaked in it, the part being first dried and then flooded with water and neutralised with dilute ammonia—Spencer, Chapman & Messel, Ltd

**Unguentum Amyl Salicylatis Compositum.** Similar to Methysal Balm *q v*, but made with amyl salicylate Odour more pleasant

**Borneol Salicylate.** *Prop Name* SALIF (*Heyden, Dresden, Braun, London*) In muscular rheumatism and acute neuralgia, by inunction or by painting over affected part Apply  $\frac{1}{4}$  to 1 drachm with equal quantity of olive oil.

**Æthylis Salicylas.**  $C_6H_4(OH)COOC_2H_5 = 166.1$ .

A colourless liquid of aromatic odour, with b.p.  $225^\circ$  to  $234^\circ$ , and properties similar to those of the methyl compound Soluble in alcohol.

**Salicyl Salicylate.** *Prop Name* DIPLOSAL (*Boehringer, Mannheim, Pharmaceutical Products, London*)  $OH C_6H_4 COO C_6H_4 COOH = 258.1$

Tablets contain  $7\frac{1}{2}$  gr *Dose*—1 or 2 tablets, 4 to 6 times daily

Salol in which the phenyl group is replaced by salicylic acid. White odourless needles melting at  $147^\circ$  Insoluble in water and dilute acids, soluble in alcohol. Used for rheumatism, neuralgia, and cystitis

Pharmacological experiments showed that the compound remained unchanged for 6 hours in the gastric juice, but was decomposed in 2 or 3 minutes in the duodenal secretion Hence it does not cause gastric disturbances

**Salicylic Ester of Dihydroxyethane.** *Syn* SED An almost odourless oily liquid consisting of a mixture of the mono-ester and di-ester It solidifies to a crystalline mass at low temperatures It contains the equivalent of about 90% of salicylic acid Insoluble in water and glycerin, soluble in other organic liquids, and in oils and fats

**Estersil** (*Johnson & Sons, London*). Ethyl and propyl esters of salicylglycollic acid, 49% of each, with oil of lavender 2%. Liquid, for external application in rheumatism.

**Mycocoten** (*Leo, Copenhagen; Bencard, London*). Preparations (powder, spirit, ointment) containing oxybenzoic acid ester and salicylic acid. Mycotic eczema.

**Salen** (*Ciba, London*). Methyl and ethyl glycollic acid esters of salicylic acid. An oily liquid for local application in rheumatic affections, etc.

**Sal-Ethyl Carbonate** (*Parke, Davis, London*). Salicylic ethyl ester carbonate in 5 gr. tablets. *Dose*.—1 to 3 tablets with water. For the relief of acute rheumatism, etc.

**Spirosal** (*Bayer Products, London*). Monoglycol salicylate. Applied externally, diluted with alcohol or olive oil, or in an ointment; as an antirheumatic.

**T.C.P.** (*British Alkaloids Ltd, London*) is stated to be a 1% aqueous solution of "trichlorophenylmethylodosalicyl" with a R W coefficient of 10 calculated on the pure salt. It is a non-toxic antiseptic advocated for local application to wounds, ulcers, boils, burns, chilblains, skin affections, insect bites and stings, nasal catarrh (diluted 1 in 2 or 3 of water) and conjunctivitis (1 in 10), etc.

**T.C.P. B3 Colloidal Emulsion** contains trichlorophenylmethylodosalicyl 1%, tribromoacetylodooxybenzoic acid 2%, T.C.P. bismuthate 1.5% colloidal aluminum silicate 2%, glycerin 3%, distilled water 90.5%. For the treatment of bacillary infections of the alimentary tract such as dysentery, colitis, gastro-enteritis, etc. *Dose*— $\frac{1}{2}$  oz in water twice a day.

**T.C.P. Ointment No. 33** contains trichlorophenylmethylodosalicyl 15, iodine (as tincture) 0.42, methyl salicylate 4, sulphur 3.5, and colloidal kaolin 22.65 with camphor, tannic acid, salicylic acid, borax, boric acid, creosote and glycerin in a paraffin base. For eczema, hæmorrhoids, chilblains and rheumatic conditions.

## ACIDUM SULPHURICUM

*B.P., U.S.P. XI, P. Dan., P. Helv. V*

$\text{H}_2\text{SO}_4 = 98.08.$

*Syn.* OIL OF VITRIOL.

[P2] "*Sulphuric acid.*"

[83] "*Sulphuric acid*—in substances containing less than 9%, weight in weight, of sulphuric acid ( $\text{H}_2\text{SO}_4$ ); accumulators; batteries; fire extinguishers."

*Dose*.—1 to 2 minims (0.06 to 0.12 ml.).

*B.P.* requires sp. gr. about 1.84, the acid containing not less than 95% w/w of  $\text{H}_2\text{SO}_4$ .

**Antidotes.** Treat as for poisoning by glacial acetic acid, see p. 7.

**Uses.** Very occasionally as caustic.

Pruritus has been treated by its internal use, even when alkaluria is absent. *Dose*, 1 tablespoonful every 2 hours of  $1\frac{1}{2}$  to  $2\frac{1}{2}\%$  solution. The itching is said to disappear rapidly.

[P2] **Acidum Sulphuricum Fumans.** *Syn.* NORDHAUSEN SULPHURIC ACID or "*Oleum*," sp. gr. about 1.9. Contains some sulphuric anhydride dissolved in sulphuric acid. When made by distillation of ferrous sulphate, ferric oxide or colcothar or polishing rouge remains behind.

"C.O.V." and "B.O.V." are impure commercial sulphuric acid, known as commercial oil of vitriol and brown oil of vitriol respectively.

**[P2] Acidum Sulphuricum Aromaticum (B P C.).***Syn.* ELIXIR OF VITRIOL.*Dose* —5 to 20 minims (0.3 to 1.2 ml.).

Contains the equivalent of about 13% *w/w* of free and combined sulphuric acid with tincture of ginger, spirit of chloroform and alcohol 90%.

**[P2] Acidum Sulfuricum Aromaticum (U.S.P. XI).***Average dose.*—8 minims (0.5 ml.)

Contains about 20% of free and combined sulphuric acid with fluidextract of ginger, oil of cinnamon and 80 to 85% by volume of alcohol.

**[P2] Acidum Sulphuricum Dilutum (B P ).**

*Dose.*—5 to 60 minims (0.3 to 4 ml.), *U S P average dose* 15 minims.

Is prepared by diluting 104 g of the strong acid with water to 1000 g. An acid of approximately the same strength is obtained by diluting 1 oz. 100 m with water to 1 pint

Contains 10% *w/w* of  $H_2SO_4$  and has sp. gr. 1.064 to 1.073; *U.S.P. XI*, *Fr Cx*, *F Norsk*, *FE VIII* and *P. Helv V* are similar, *P Ned V* is 4N, *i.e.*, 19.6%, *P.G. VI* 15.6 to 16.3%, *P Ital. V* approx 19%, *P Belg* approx 9.8%; *P. Dan* 9.2%.

**Incompatible** with alkalis and carbonates. It precipitates barium and calcium from solutions of their salts, also soluble lead and silver salts

**Uses.** Similar to those of other mineral acids. Antiseptic and astringent in diarrhoea. In cholera epidemics "sulphuric acid lemonade," containing 5 to 10 m of dilute acid per pint of sweetened water, has been taken as preventive; it is also taken by lead workers as preventive of plumbism. Dilute sulphuric acid in 20 to 30 m. doses, well diluted, every 4 hours is of value in carbuncles, boils and staphylococcal infections. Cases of bronchiectasis and pulmonary tuberculosis where there is often a staphylococcal infection have also benefited

**Linctus Acidus (B.P.C.).***Dose* — $\frac{1}{2}$  to 1 drachm (2 to 4 ml.)

Oxymel 1 in 3 with dilute sulphuric acid, emulsion of chloroform and treacle

**[P1] Mistura Acidi Sulphurici cum Opio (B P C )***Dose* — $\frac{1}{2}$  to 1 ounce (15 to 30 ml.)

Contains dilute sulphuric acid 20 m and tincture of opium 7  $\frac{1}{2}$  m. with tincture of capsicum and camphor water to 1 oz

**Ammonii Sulphas.  $(NH_4)_2SO_4$  - 132.1**

Colourless crystals soluble about 3 in 4 of water. It is made by distilling gas liquor with lime into sulphuric acid and is a source of ammonia for refrigeration and similar purposes. Its chief use is as a fertiliser and for fire proofing. It is also used for precipitating proteins from solution

**Potassii Sulphas (B.P.C., P. Helv V, P. Dan.).***Syn.* SAL POLYCHRESTUM.  $K_2SO_4 = 174.3$ .*Dose.*—15 to 45 grains (1 to 3 g.)



Colourless crystals with saline, slightly bitter taste Soluble 1 in 10 of water A saline purgative.

0.25 to 0.5% added to local anæsthetics, whether by spinal injection or peripheral blocking of nerves, enhances anæsthesia

**Sodii Sulphas** (*B.P.*, *U.S.P. XI*, *P. Dan.*)

*Syn.* GLAUBER'S SALT  $\text{Na}_2\text{SO}_4 \cdot 10\text{H}_2\text{O} = 322.2$ .

*Dose* — $\frac{1}{2}$  to 4 drachms (2 to 16 g.) *U.S.P. XI* average dose 4 drachms.

The form known as "feathery crystals" is handy for dispensing.

**Soluble** about 1 in 3 of water, also in glycerin, insoluble in alcohol.

**INFANTILE DIARRHŒA**—Small doses have been advised—about 6 gr. initially for a baby under 6 months, in dill water Children over 6 months can take 10 to 20 gr. without producing aperient action

**WOUNDS**—Plain lint soaked in a 12% solution of sodium sulphate and applied to the surface of any ordinary, fairly open septic wound is astonishingly effective and is preferable to the use of antiseptics The lint is covered with oiled silk or elastic adhesive plaster and bandaged The lint must be kept soaked with the solution and changed twice a day or more often if necessary One of the first and almost immediate symptoms is the relief of pain—*J. C. Lyth, Brit. med. J.*, 11/1935, 905

**Sodii Sulphas Effervescens** (*B.P.*)

*Dose*.—1 to 4 drachms (4 to 16 g.)

Contains 50% of sodium sulphate.

A teaspoonful or more in half a tumbler of water, taken half an hour before breakfast, is an efficient evacuant

**Sodii Sulphas Exsiccatus** (*B.P.C.*, *P. Helv. V*, *P. Dan.*)

$\text{Na}_2\text{SO}_4 = 142.1$

*Dose* — $\frac{1}{2}$  to 2 drachms (1 to 8 g.)

A white powder readily absorbing moisture On drying, crystalline sodium sulphate loses about half its weight

**Soluble** 1 in 8 of water.

**Sal Carolinum Factitium** (*B.P.C.*) *Syn.* ARTIFICIAL CARLSBAD SALT

*Dose*.—1 to 2 drachms (4 to 8 g.)

A crystallised preparation containing sodium sulphate about 55% with potassium sulphate, sodium chloride and sodium carbonate  $1\frac{1}{2}$  drachms is approximately equivalent to 1 pint of the natural water

**Sal Carolinum Factitium** (*P.G. VI*, *P. Ned. V*, *P. Belg. IV*)

*Dose* —20 to 60 grains (1.3 to 4 g.)

A powdered preparation containing exsiccated sodium sulphate 22, potassium sulphate 1, sodium chloride 9, sodium bicarbonate 18.5 gr. is approximately equivalent to 1 pint of the natural water

*P. Helv. V* and *P. Dan.* are similar

**Sal Carolinum Factitium Effervescens** (*B.P.C.*)

*Syn.* EFFERVESCENT CARLSBAD POWDER

*Dose*.—1 to 2 drachms (4 to 8 g.)

Contains about 10% of exsiccated sodium sulphate and 40% of sodium potassium tartrate

**Sodii Magnesii Sulphas Effervescens** (*Martindale, London*)

*Dose* —A teaspoonful or more in half a tumbler of water taken half an hour before breakfast "Vescettes" of this preparation contain 60 grains

**Sodii-Magnesii Sulphas Effervescens cum Caffeina** (*Martindale, London*) *Dose*—One teaspoonful or more “Vescettes” of this preparation contain 60 grains in each. A useful “pick-me-up” and for headaches.

**Chloro-Sodio-Magnesian Aperient** (*Martindale, London*)

*Dose*—A teaspoonful or more.

An efficient saline purge, useful taken in migraine and other forms of headache, also in constipation, and for assisting digestion and relieving depression by increasing the action of the liver, intestines, and kidneys, and promoting free excretion of waste products.

**Marienbad salt** is similar to powdered artificial Carlsbad salt. **Marienbad salt tablets** may be prepared containing 60 grains of the mixture.

**Marienbad Antiobesity Tablets.** *Dose*—One or two at bedtime. Aloes  $\frac{1}{2}$  gr., rhubarb 1 gr., cascara extract  $\frac{1}{2}$  gr., Marienbad salt  $\frac{1}{2}$  gr., fucus extract  $\frac{1}{2}$  gr.—*Pharm J Formulary*

**Sal Emsarum Facticum** (*P Ned V*) Exsiccated sodium sulphate 10, potassium sulphate 10, sodium chloride 265, sodium bicarbonate 7.5.

**Sal Hunyadi Janos Facticum** (*P Ned IV*). Magnesium sulphate 950 exsiccated to 500, sodium chloride 50, exsiccated sodium sulphate 450.

**Sal Vichy Facticum** (*P Ned V, P Helv V*) Sodium phosphate (cryst.) 20, potassium sulphate 50, sodium chloride 80, sodium bicarbonate 850.

**Sal Wildungense Facticum** (*P Ned V*) Potassium sulphate 5, calcium carbonate 190, magnesium carbonate 190, sodium chloride 240, sodium bicarbonate 375. To make artificial Wildungen water use 4.6 g per litre.

*Dose* of each—20 to 60 grains (1.3 to 4 g), increased as required.

**Sodii Sulphas Acidus**, *syn* SODIUM BISULPHATE,  $\text{NaHSO}_4 \cdot \text{H}_2\text{O}$ , occurs in crystals or fused masses. Is used for preparing effervescing baths.

**Nauheim Bath Salts** are prepared with this salt and sodium bicarbonate. The Nauheim water contains in addition sodium and calcium chlorides.

**Ammonii Persulphas** (*B P C*)  $(\text{NH}_4)_2\text{S}_2\text{O}_8 = 228.2$ .

White crystals obtained by the electrolysis of ammonium sulphate solution. Soluble 1 in 2 of water. Is used in the preparation of the persulphates.

**Potassii Persulphas** (*B P C*)  $\text{K}_2\text{S}_2\text{O}_8 = 270.3$

White crystals soluble 1 in 3 of water. A bleaching agent; used also in photography as a reducer. Its use as a flour “improver” is liable to cause “baker’s itch.”

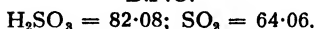
**Sodii Persulphas.**  $\text{Na}_2\text{S}_2\text{O}_8 = 238.1$

*Dose*—1 to 3 grains in water before meals.

In small white granular crystals, soluble in water. In tuberculosis and chlorotic and neuropathic subjects stimulates appetite. Useful in hyper-acid dyspepsia at the onset, also in gastric cancer. A strong oxidising and bleaching agent.

Intravenous injection of fresh 5% sodium persulphate solution, 60 ml each day, preferably in 2 or more doses injected slowly, the injection taking some 5 minutes, has given good results in tetanus. A reaction often appears—nausea and vomiting for  $\frac{1}{2}$  hour.

Liberates about 13% active oxygen. If it is desired to avoid production of free sulphuric acid, the persulphate may be mixed with  $1\frac{1}{4}$  times its weight of sodium carbonate. 3 to 10% solutions as gargle and dressing. Suitable for wounds requiring moist dressing and where disinfection necessary. For small ulcers may be used as dusting powder, with equal quantity of powdered talc. Odourless and non-toxic.

**ACIDUM SULPHUROSUM***B.P.C.*

**Dose.**— $\frac{1}{2}$  to 1 drachm (2 to 4 ml.).

A colourless liquid, with strong sulphurous odour, and containing 5% of  $\text{SO}_2$ . Sp. gr. about 1.025

**Preparation.** By roasting sulphur or by heating copper and sulphuric acid, or carbon and sulphuric acid, and dissolving the gas in water. Sulphur dioxide is also available compressed in cylinders.

**Antidotes.** Keep patient warm; mustard plaster on chest. Give narcotics if necessary. Artificial respiration.

**Uses.** This solution of sulphurous acid is applied externally as a lotion—one part to two or more of water and sometimes a little glycerin added for affections such as chloasma, ringworm, pruritus, thrush and chapped hands, with very good results. It is sprayed into the throat for tonsillitis, diphtheria (better diluted) and asthma, or used as an inhalation, a teaspoonful to a pint of cold water. It is strongly antiseptic, and has been used in whooping cough by fumigating the room. Also diluted, for fœtor of the teeth, e.g. in syphilis.

Internally it has been used in cholera (freely diluted). As a rectal injection, a 1 or 2% solution of the gas. Also for gastric fermentation accompanied by sarcinæ, and in typhoid (20 to 30 minim doses, diluted) every 2 or 3 hours.

**Lotio Acidi Sulphurosi (B.P.C.).**

Sulphurous acid and glycerin of tannic acid, of each 1 in 4 in distilled water. Useful as a paint or spray in tonsillitis and septic sore throat.

**Magnesi Sulphis.**  $\text{MgSO}_4 \cdot 6\text{H}_2\text{O} = 212.5$ .

**Dose**—10 to 30 grains (0.6 to 2 g.)

White crystalline powder. Soluble 1 in 90 of water. Given in diphtheria and other infectious diseases. Large doses may be given with impunity.

**Magnesi Thiosulphas.** *Syn* MAGNESII HYPOSULPHIS.

$\text{MgS}_2\text{O}_3 \cdot 6\text{H}_2\text{O} = 244.5$ .

**Dose**—8 to 15 grains (0.5 to 1 g.) orally, or by intramuscular injection of a 10% solution.

Colourless crystals soluble 1 in  $1\frac{1}{2}$  of water. Used in the treatment of allergic diseases.

Spasmodic coryza and asthma, resistant cases successfully treated by magnesium thiosulphate tablets 0.5 g., 4 to 6 daily, or the intramuscular injection every fourth day for 2 weeks of 10 ml. of a 10% solution. Injections stated to be painless and amelioration of symptoms to follow almost immediately—G. Boissel, *Pr med*, May 17, 1930.

Asthma of 2 to 25 years' standing treated *per os*. Results satisfactory, no contraindications—M. J. Fenton, *Brit. med J.*, ii/1930, 940.

**Emgé** (*Lumière, Lyons, Anglo-French Drug Co, London*) Ampoules containing 10 ml of 10% magnesium thiosulphate solution for intramuscular injection in the treatment of all anaphylactic reactions.

Tablets for oral administration contain 0.6 g. of magnesium thiosulphate with 0.2 g. of magnesium silicate to neutralise the laxative effect. Stated to stimulate the secretion of intestinal enzymes and thus improve digestion.

**Magnesium Hyposulphite Sterules** (*Martindale, London*) contain 10 ml. of 10% solution

**Sodii Sulphis** (*B.P.C.*).  $\text{Na}_2\text{SO}_3 \cdot 7\text{H}_2\text{O} = 252.2$ .

*Dose* —5 to 20 grains (0.3 to 1.2 g.).

Colourless efflorescent crystals slowly oxidising in air to sulphate (keep in stoppered bottles).

**Soluble** 1 in 2 of water, 1 in 25 of glycerin; slightly in alcohol 90%. Incompatible with acids. Antiseptic.

In dilatation of the stomach the late Sir Wm. Broadbent recommended as antiseptic treatment sodium sulphite 5 to 10 gr doses, with sodium bicarbonate and nux vomica between meals

As a lotion for skin affections and sores of the mouth, and internally for *sarcinæ* in the stomach

**Sodii Sulphis Exsiccatus** contains about 90% of  $\text{Na}_2\text{SO}_3 = 126.1$ . Is used in photography. Being in dry powder is convenient for transit.

**Sodii Pyrosulphis.**  $\text{Na}_2\text{S}_2\text{O}_5 = 190.1$  *Syn* SODIUM METABISULPHITE, SODIUM BISULPHITE.

Made by passing sulphur dioxide into a hot concentrated aqueous solution of sodium sulphite.

Prismatic crystals or white powder readily soluble in water

The true bisulphite or acid sulphite,  $\text{NaHSO}_3$ , does not exist as a solid

A solution of sodium pyrosulphite 20 gr in alcohol 90% 1 oz., peppermint oil 5 m, and glycerin 2 oz has been used as an antiseptic throat pigment. In photographic use sodium pyrosulphite is similar to the potassium salt Is largely used as a food preservative.

**Sodii Thiosulphas** (*B.P Add, U.S.P. XI, P. Helv. V, P. Dan, P. Ital. V, and F.E. VIII*) *Syn* SODII HYPOSULPHIS

$\text{Na}_2\text{S}_2\text{O}_3 \cdot 5\text{H}_2\text{O} = 248.2$ .

*Dose* —5 to 20 grains (0.3 to 1.2 g.), or more, *per os*. *B.P Add* gives dose by subcutaneous, intramuscular or intravenous injection, 5 to 15 grains (0.3 to 1 g.) Is usually injected as a 10% solution.

Crystals soluble 5 in 3 of water; insoluble in alcohol.

**Uses.** Given internally as purgative and anti-putrescent As a lotion, 1 in 10 for chloasma, ringworm, etc. Intravenously it is used for the prevention and treatment of stomatitis due to injections of mercury, bismuth or arsenic compounds, and also for the dermatitis sometimes caused by injections of gold compounds. For these purposes oral administration is less effective, but gold dermatitis may yield to a short course of 10 gr. doses thrice daily Tissue reactions due to extravenous leakage of organic arsenicals may be treated by infiltration of a 10% sterile solution.

BURNS, AND DERMATITIS CAUSED BY ARSENIC AND MERCURY —Moist applications of a 1 or 2% solution of sodium thiosulphate beneficial in treatment —*J. Amer med Ass*, 11/1925, 636

**DISTEMPER** in dogs is well treated by sodium thiosulphate. First give a purgative of  $4\frac{1}{2}$  to  $7\frac{1}{2}$  grains each of calomel and scammony, then the thiosulphate 9 to 15 grains in milk or sugar and water next day for 10 days

**ECZEMA**—0.45 to 0.75 g intravenously repeated daily without danger for weeks at a time—*Lancet*, 1/1931, 649

**PELLAGRA**—Even advanced cases cured by intravenous injections of 10 ml 10% solution, 20 to 60 injections necessary. No complications—*I. Sabry, Lancet*, 11/1931, 1022, *J trop Med (Hyg)*, Sept, 1931, 303

**Intravenous Use in Mercurial and Bismuth Stomatitis and Arsenical Poisoning.**—In dose of 3 to 4 injections of 0.45 to 0.6 g in 5 ml of water intravenously, alternate days, it is potent—possibly for all acute metal poisoning. Stated to be non-toxic up to 2 g doses—*H C Semon, Brit med J*, 1/1924, 664

Mercurial stomatitis and a case of tissue reaction due to leaking of neoarsphenamine from a vein treated by 0.45 g of thiosulphate in 10 ml, 0.6 g given prior to arsphenamine was followed by slight rigor—*China med J*, Sept 1925, per *Chem. & Drug*, 11/1925, 899.

Antidotal action in mercuric chloride or mercurochrome poisoning not substantiated—*K I McIlville and M Bruger, J Pharmacol*, Sept, 1929, 7, Mendelson, per *Prescriber*, 1928, 349

For inorganic arsenicals valueless *per os*—*J Amer med Ass*, 1/1927, 1220

Potassium cyanide poisoning. Two injections of 10 ml 30% of value—*Per J. Amer med Ass*, 1/1927, 1525. 1 g intravenously—*Klin Wschr*, July, 1928, 1351

In the later treatment of arsenic and mercury poisoning not of much value. Liver extract of value in Salvarsan dermatitis. Intramuscular injections of 5 to 10 ml of a 1=1 preparation—*Lancet*, 1/1929, 1102

Has no effect as an antidote in arsenical poisoning whether administered orally or intravenously—*P Scaduto, Arch int Pharmacodyn*, 1931, 4, 290

**Calcium Thiosulphate.** Arsenical or bismuth dermatitis treated by 0.6 g daily intravenously of a 10% solution for 3 days and then bi-weekly injections. Exerted definite curative influence in 6 cases—*A E W McLachlan, Brit med J*, 1/1933, 916

**Ametox** (*Pharmaceutical Specialties (May & Baker) Ltd, London*)

Preparations of sodium thiosulphate, calcium thiosulphate or magnesium thiosulphate. The sodium thiosulphate preparation is available in ampoules of solution or of the exsiccated salt. The calcium and the magnesium preparations are in ampoules of solution, the latter also in tablets for gastric fermentation

**Calciostab** (*Boots, Nottingham*)

10% aqueous solution of calcium thiosulphate, for the prevention and treatment of metallic poisoning from antisyphilitic treatment. Dose—6 ml intravenously daily up to the seventh or eighth day and then every second or third day

**Thiostab** (*Boots, Nottingham*)

Sterile 10% solution of sodium thiosulphate in ampoules containing 0.3 to 0.9 g of exsiccated salt (equivalent to 0.45 to 1.35 g of the crystalline compound)

**Sodii Hydrosulphis.**  $\text{Na}_2\text{S}_2\text{O}_4 = 174$

White powder soluble in water with evolution of  $\text{SO}_2$ . An active reducing agent used in manufacturing processes

**ARSENICAL POISONING.**—100 mg per kilo weight *per os* enabled animals to survive fatal doses of arsenic. Low toxicity but may cause vomiting. Best given in a fresh solution followed by 25 ml of normal hydrochloric acid—*W R. Bond and E W Gray, J Amer. med Ass*, 1/1929, 1919

## ACIDUM TANNICUM

*U S P XI, F F VIII, P. Belg. IV, P Ital V, P. Dan., P. Helv. V.*

$\text{C}_{14}\text{H}_{10}\text{O}_9 = 322$  1.

*Syn* TANNIN

Dose.—5 to 10 grains (0.3 to 0.6 g.). *U.S.P average dose* 15 grains

Extracted from specially fermented galls with ether containing a little alcohol and water.

**Soluble** in water 1 in 1 slowly, in glycerin 1 in 1, and in alcohol 90% 1 in 1. Almost insoluble in ether, chloroform, benzene and light petroleum.

**Incompatible** with ferric salts, acids, alkalis, silver and other metals and with gelatin. Furthermore, tannin solution precipitates the majority of alkaloids from solution, hence is occasionally employed as an antidote to these.

**Uses.** Throat and mouth wash 1 to 2%. Astringent and styptic in powder form for epistaxis (by coagulating the albumin). Sometimes given in dysentery. Rectal injection of 30 grains in a quart of hot water, with or without opium, has been given in cholera. It is a useful astringent applied to the gums and as an ingredient in tooth powders.

**ECZEMA**—For the treatment of weeping eczema it is recommended to start with a 10% solution to give quick relief, followed by a weaker solution down to 2.5%, discontinued when the weeping surface has dried, it is unnecessary to carry the treatment to the tanning stage. A bland ointment containing zinc oxide, tar, starch, and soft paraffin is then applied.—P. S. Tennant, *Canad med Ass J*, Oct., 1934, 414.

Also of value in impetigo neonatorum, the vesicles being ruptured with a swab dipped in 10% solution, followed by swabbing the areas with a 2.5% solution several times daily for 2 days.—*ibid*.

### **Tannic Acid Treatment of Burns.**

First advocated by E. C. Davidson (*Surg Gynec Obstet*, 1925, 12, 202) and results confirmed by W. C. Wilson (*Spec Rep Ser med Res Coun., Lond*, No 141, 1929). A 2% solution of tannic acid (originally 2½% was used) with 1-2000 of mercuric chloride is applied warm on lint wrung lightly out of the solution, the dressing being completed by covering with wool and bandaging in position. For hospital treatment the burned area should be sprayed with the solution and dried—by electric lamps in bed cases or by an electric drier—the application being repeated every hour until a thin brown layer of coagulated tissue is formed (7 to 10 applications). In face burns, the solution must be prevented from entering the eyes, to avoid coagulation of the cornea. The area round the eyes should be smeared with soft paraffin and covered with cotton wool. No part of burnt area should touch bedclothes or bed. The solution should be freshly prepared since the coagulating power decreases on keeping.

At St. Thomas's up to 1900, mortality from burns and scalds was 23 to 24% of the cases occurring annually, this was reduced to 14% with the introduction of the picric acid method, and with the introduction of the tannic acid treatment in 1928 was further reduced to 4% in 1929, 3% in 1930, 2½% in 1931, and nil in 1932 (up to October). A moderately large dose of morphine should be given at the earliest possible moment to minimise primary shock.—N. Lock, *Brit med. J*, 1/1933, 272. See also P. H. Mitchiner, *ibid*, 447, and *Lancet*, 1/1933, 233.

An improvement on the usual spray of 5% tannic acid solution is to follow this by the application of 10% silver nitrate solution. Minimises shock and toxæmia and promotes more rapid healing.—A. G. Bettman, per *Prescriber*, 1935, 304.

A 20% solution, which produces immediate coagulation, has many practical advantages over a 2.5 or 5% solution. An antiseptic—1 in 1000 acriflavine or

1% aqueous solution of gentian violet—should be incorporated in the coagulating solution or applied immediately afterwards—W C Wilson, *Practitioner*, 1/1936, 398.

**MISUSE OF TANNIC ACID**—The tannic acid treatment of burns was originally advocated for use in severe, extreme cases. It is now frequently used in milder "second degree" burns. Any surviving epithelial cells that might take part in the repair of the denuded area are all "tanned" by the treatment. Repair is thus delayed. It is suggested that coagulation treatment of burns be reserved for the most severe types and that bland wet dressings and ointments be used on the great majority of "second degree" burns—F Taylor, *J Amer med Ass* 1/1936, 1144.

**DISADVANTAGES OF TANNIC ACID TREATMENT**—The coagulum is coarse, tough, and not transparent, the acid is "dirty" and destructive to clothing and bed linen, it is unstable in aqueous solution and its employment cumbersome. A 2% aqueous solution of mercurochrome is better (*see mercurochrome*)—A C Turner, *Brit. med J*, 11/1935, 995.

**Collodium Stypticum** (*B.P.C.*) contains 15% *w/v* of tannic acid with benzoin and alcohol in simple collodion.

**Gargarisma Acidi Tannici** (*B.P.C.*) contains 12½% of glycerin of tannin.

**Glycerinum Acidi Tannici** (*B.P.*).

*Dose.*—10 to 30 minims (0.6 to 2 ml.).

Tannic acid 15% *w/w* in glycerin.

**Glyceritum Acidi Tannici** (*U.S.P. XI*).

Tannic acid in glycerin 1 in 5 by weight, with 1% of sodium citrate.

[P2] **Lotio Acidi Tannici** (*B.P.C.*).

Tannic acid 2% *w/v* and mercuric chloride 1 in 2000 in distilled water. For the treatment of burns.

**Lotio Acidi Tannici** (*Mid. H.*)

Tannic acid 10 gr, resorcinol 4 gr, spirit of rosemary 1 dr, water to 1 oz. For only seborrhœa.

**Pessus Acidi Tannici** (*B.P.C.*) contains 10 gr. (0.6 g.)

**Pulvis Acidi Tannici et Acriflavinae** (*C.X.H.*)

Tannic acid 30 gr, acriflavine 1½ gr, warm sterile water to 3½ fl oz. To be dissolved immediately before use and applied with a sterile brush, or on gauze, or as a spray.

[P2 81] **Solvellæ Acidi Tannici Compositæ** (*B.P.C.*)

One solution-tablet dissolved in 1 fl oz of water gives a solution of about the same strength as the *B.P.C.* lotion.

**Suppositorium Acidi Tannici** (*B.P.*)

3 grains (unless otherwise stated), with theobroma oil *q.s.* to 15 grains.

[D P1 81] **Suppositories of Tannic Acid with Opium**, 1 grain in addition, or [D P1 81] morphine ½ gr.

**Trochiscus Acidi Tannici** (*B.P.*) Each contains ½ grain (0.03 g.).

**Unguentum Acidi Tannici** (*B.P.*).

Tannic acid 20, in glycerin, yellow beeswax and benzoated lard to 100.

**Unguentum Acidi Tannici** (*U.S.P. XI*).

Tannic acid 20, glycerin 20, wool fat 3, yellow wax 3, petrolatum 54.

**Amertan** (*Lilly, London*) A non-greasy jelly containing 5% tannic acid and Merthiolate (*q.v.*) 1 in 5000. For the treatment of burns.

[P1] **Tanichthol Suppositories** (*Sharp & Dohme, London*). Contain tannic acid  $2\frac{1}{2}$  gr., phenol  $\frac{1}{2}$  gr., ichthyol 1 gr., extracts of stramonium, belladonna and witch hazel of each  $\frac{1}{2}$  gr. in a glycerin base. Haemorrhoids, anal fissure and fistula, and chronic inflammatory conditions of the rectum, anus and vagina.

**Tannafax** (*Burroughs Wellcome, London*). Tannic acid with 0.5% phenol in a water-soluble base. For burns and scalds, apply lightly, allow to dry and bandage loosely.

**Tannaflavine** (*British Drug Houses, London*). Combination of tannic acid and acriflavine. Contents of one tube make  $\frac{1}{2}$  pint of solution containing  $2\frac{1}{2}\%$  of tannic acid and 0.1% of acriflavine.

### **Aluminii Tannas.** *Syn.* TANNAL INSOLUBILE

$Al_2(OH)_4(C_{14}H_9O_2)_2 \cdot 10H_2O$ . Is made by precipitating a solution of aluminium trisulphate with sodium tannate, or better by treating freshly made aluminium hydroxide with tannin solution. As astringent for chronic catarrh of the respiratory organs.

**Albuminum Tannicum** (*U.S.P. XI, P. Belg. IV, P. Jap., F.E. VIII, P. Austr., P. Ned. V with method of making*). *Prop. Name* TANNALBIN (*Knoll, Ludwigshafen; Pharmaceutical Products, London*).

*Dose.*—8 to 15 grains (0.5 to 1 g.). *U.S.P. XI* average dose 30 grains.

A compound of tannin with albumen, in pale brown, insoluble, tasteless powder.

*Uses.* A disinfectant soluble in the intestines but unaffected by the stomach, given for diarrhoea.

**Tannocarbon** (*Richter, London*). Tablets containing tannin albuminate 2 gr., charcoal 2 gr. *Dose.*—1 or 2 tablets thrice daily. Flatulence, dysentery, mucous colitis.

### **Zinci Tannas.** *Syn.* "SEL DE BARNIT."

Is obtained by treating zinc oxide 10 in water 15 with tannin 50 in alcohol (45%) 100. Dry at gentle heat.

Used as ophthalmic application and for decubitus and other skin lesions.

**Acetannin** (*B.P.C, P.G. VI, etc*) *Syn. and Prop. Name.* DIACETYL-TANNIN, ACIDUM ACETYLTANNICUM, TANNYL ACETATE, TANNIGEN (*Bayer Products, London*).

$C_{14}H_8(COCH_3)_2O_9 = 406$  l.

*Dose*—5 to 10 grains (0.3 to 0.6 g.) in cachet.

**Manufacture.** Tannic acid 10 g., acetic anhydride 15 ml.; heat on water-bath 1 hour. Add 25 ml. of alcohol and pour the solution into 500 ml. of water, collect, wash and dry at not exceeding  $60^\circ$ —C. E. Corfield and G. R. A. Short, *Pharm. J.*, 11/1924, 115.

A yellowish or greyish white tasteless powder. Almost insoluble in water, alcohol or ether; soluble in ethyl acetate, and in alkalis with decomposition. *P.G. VI* defines it as mainly a mixture of diacetyl and triacetyltannin.

In diarrhoea. Dissolves in the intestine, appearing in the urine as gallic acid. Should not be prescribed with alkali.

**Methyleneditannin** (*P.G. VI*). *Syn. and Prop. Name.* METHYLEDITANNIN, TANNOFORM (*Merck, Darmstadt; Martindale, London*).



A compound of tannin with formaldehyde in reddish-white powder insoluble in water, soluble in alcohol and alkalis. Used as an antiseptic in ointment (1 in 10) or dusting powder, alone or with 1 to 4 parts of starch, for bedsores, hyperhidrosis, pruritus, eczema (particularly in interdigital eczema), piles and tender feet. Internally in diarrhoea and enteritis, in doses of 8 to 15 gr.

**Acidum Gallicum** (*B.P.C.*, *P. Helv.* V) *Syn* ACIDO AGALICO (*F.E. VIII*).  $C_6H_2(OH)_3COOH, H_2O = 188.1$

*Dose* —5 to 15 grains (0.3 to 1 g.)

Crystals or crystalline powder of brownish colour

**Soluble** about 1 in 100 of water, 1 in 6 of warm glycerin, 1 in 3 of alcohol 90%. Properties and uses similar to those of tannic acid, *q.v.*

**Glycerinum Acidi Gallici** (*B.P.C.*).

*Dose* —10 to 60 minims (0.6 to 4 ml.)

About 1 in  $6\frac{1}{2}$  w/w. Used in the same way as Glycerinum Acidi Tannici

**Galla** (*B.P.C.*, *U.S.P. XI*, *P. Helv. V*, *P. Dan.*)

*Dose*.—10 to 20 grains (0.6 to 1.2 g.) *U.S.P. XI* average dose 8 grains

Excrescences on *Quercus infectoria* (Fagaceæ) caused by deposition of eggs of *Cynips gallæ tinctoriæ* (Cynipidæ). Astringent. Contains 50 to 70% of gallotannic acid.

**Tinctura Gallæ** (*B.P.C.*). *Dose* — $\frac{1}{2}$  to 2 drachms (2 to 8 ml) 1 in 8 of alcohol 60%.

**Unguentum Gallæ** (*B.P.C.*) 20%

**Unguentum Gallæ** (*U.S.P. XI*)

Nutgall 20, wool fat 5, yellow wax 5, petrolatum 70

[**Pi 81**] **Unguentum Gallæ cum Opio** (*B.P.C.*) Unguentum Gallæ (*B.P.C.*) with addition of  $7\frac{1}{2}\%$  of powdered opium (*Exempt D*).

**Skol** (*Skol Products, London*). Extract of galls 5, menthol 0.25, phenol 0.5, glycerin 3, salicylic acid 1, alcohol and water to 100. A healing antiseptic for use in burns, bed-sores, cuts, stings, etc.

**Æsculus Hippocastanum.** *Syn* HORSE CHESTNUT, MARRON D'INDE (*Fr. Cx. Supp.* 1926). Tincture of seeds 1 in 10 of proof spirit has been given for painful hæmorrhoids. *Dose* —10 minims night and morning. Also emmenagogue. A liquid extract has been used, painted on or rubbed in, in rheumatism and neuralgia.

**Æsculin**,  $C_{18}H_{16}O_8, 1\frac{1}{2}H_2O = 367.1$ , a glycoside, soluble in water to which 2 to 3% sodium carbonate is added, also soluble in alcohol. Solutions have a blue fluorescence, and have been used similarly to quinine in X-ray and Finsen light treatment (*q.v.*). *Dose* —1 to 5 minims of 5% solution.

An ointment containing æsculin 2% in soft paraffin or other base may be used for prevention of sunburn.

**Hæmatoxylin** (*B.P.C.*) *Syn* LOGWOOD. The unfermented heart-wood of *Hæmatotoxylon campechianum* (Leguminosæ). Contains 10% of hæmatoxylin, and tannin. Is used as an astringent, and the decoction is also used for some forms of urinary hæmorrhage.

Preparations of logwood colour the fæces and urine red, and stain linen. The fermented chips used by dyers are deep red in colour, have lost the sweet taste and the hæmatoxylin is oxidised to hæmatein,  $C_{18}H_{12}O_8$ .

**Decoctum Hæmatoxyli** (B P C). Dose— $\frac{1}{2}$  to 2 ounces (15 to 60 ml.). 1 in 20 with 1% of cinnamon

**Extractum Hæmatoxyli.** Dose—5 to 15 grains (0.3 to 1 g) A soft aqueous extract

**Extractum Hæmatoxyli Liquidum** (B P C) Dose— $\frac{1}{2}$  to 2 drachms (2 to 8 ml) 1 in 1

**Hæmatoxylin.**  $C_{16}H_{14}O_6 \cdot 3H_2O = 356.2$  Usually in yellowish granular crystals, slowly soluble in water, easily in alcohol. Alcoholic solution 0.2% is used as indicator—yellow in acid and purple in alkaline solution

**Decoctum Sappan** 1 in 20 of sappan wood, *Cesalpinia Sappan* (Leguminosæ), is similar to decoction of logwood

**Myrobalanum** (B P C) Syn BLACK OR CHIBULIC MYROBALANS The dried immature fruits of *Terminalia Chebula* (Combretaceæ) Contain 20 to 40% of tannin Used as an equivalent of gall in India and the East

It is a valuable styptic Is purgative in large doses ( $\frac{1}{2}$  to 2 dr), but may constipate after purging The natives employ it in perineal injuries caused during childbirth, also in eczematous sores and prolapsus ani

Unguentum Myrobalani and Unguentum Myrobalani cum Opio are similar to the corresponding preparations of gall

**Quercus** (B P C) Syn OAK BARK The dried bark of the British oak, *Quercus Robur* and *Q. sessiliflora* (*Q. sessiliflora* and *Q. pedunculata*, P. Helv V) (Fagaceæ) Contains 15 to 20% of quercitanic acid.

**Decoctum Quercus** (B P C) About 1 in 15 Has been used as a rectal injection for hæmorrhoids and as an astringent gargle

## ACIDUM TARTARICUM

B.P., U.S.P. XI, P. Helv V, P. Dan.

$(CHOH \cdot COOH)_2 = 150.05.$

Dose—5 to 30 grains (0.3 to 2 g)

**Soluble** 10 in 8 of water, 1 in  $2\frac{1}{2}$  of alcohol 90%, 1 in  $4\frac{1}{2}$  of glycerin, 1 in 120 of ether 0.720, 1 in 5 of dehydrated alcohol Nearly insoluble in benzene and chloroform

**Incompatible** with carbonates, and with potassium, calcium and mercury salts

**Antidotes.** Give calcium hydroxide or magnesium hydroxide, stirred up in water, freely Empty stomach by stomach tube, using lime water Purgative dose of castor oil

**Uses.** For making effervescent preparations, effervescent tablets, and cooling drinks If not neutralised, it must be taken well diluted

**Ammonii Tartras.**  $(CHOH \cdot COONH_4)_2 = 184.1$

White efflorescent crystals soluble in water.

**Liquor Ammonii Tartratis** (R L O H)

Contains 20 or 40 gr. of neutral ammonium tartrate per oz. of sterilised water. For treatment of lime burns of the eye by irrigation

Lime burns of the eye. Daily irrigation for a period of 15 minutes with a 10% solution of neutral ammonium tartrate recommended. Stated to dissolve the calcium carbonate formed in the tissue—*Lancet*, 1/1926, 1212

**Potassii Tartras** (B.P.C.). Syn. NORMAL OR NEUTRAL POTASSIUM TARTRATE.  $(CHOH \cdot COOK)_2 \cdot H_2O = 470.5.$

Dose.— $\frac{1}{2}$  to 4 drachms (2 to 16 g.).

Crystalline powder with bitter taste made by neutralising acid

potassium tartrate with potassium carbonate. Has purgative and diuretic properties

**Soluble** about 5 in 3 of water.

**Potassii Tartras Acidus** (*B.P., P. Helv. V*) *Syn.* POTASSII BITARTRAS (*U.S.P. XI*), PURIFIED CREAM OF TARTAR  
 $\text{COOH}(\text{CHOH})_2\text{COOK} = 188.1$ .

*Dose*—15 to 60 grains (1 to 4 g.). *U.S.P. XI* average dose 30 grains.

Obtained by recrystallising the crude tartar (argol) deposited during the fermentation of grape-juice. A white powder with acid taste soluble 1 in 220 of water, 1 in 16 of boiling water, insoluble in alcohol 90%. Diuretic and cathartic, useful in drop-sical conditions. Is employed in acute renal disease.

BOILS AND CARBUNCLES have been treated by cream of tartar powder as a dressing. Renewed from time to time and irrigated with sterile water.

**Collutorium Acidi Tartarati** (*R.D.H.*)

Potassium acid tartrate 2 gr., tartaric acid 1 gr., syrup of lemon 3 m., saccharin  $\frac{1}{2}$  gr., water to 1 oz. Use 1 tablespoonful in half a tumblerful of water

**Potus Imperialis** (*B.P.C.*). *Syn.* HAUSTUS IMPERIALIS.

Contains 2 grains of potassium acid tartrate per fl. ounce, with citric acid, oil of lemon, tincture of lemon and water

*U.C.H.* has potassium acid tartrate 1 dr., sugar 4 dr., boiling water 1 pint. *Mid. H.*—Potassium acid tartrate 1 dr., tartaric acid 10 gr., soluble saccharin 1 gr., oil of lemon 3 m., water to 20 oz. *L.H.*—Potassium acid tartrate 40 gr., lemon juice  $\frac{1}{2}$  oz., syrup  $\frac{1}{2}$  oz. (omit for diabetic patients), water to 20 oz. *K.C.H.*—Potassium acid tartrate 1 dr., tartaric acid 1 dr., oil of lemon 1  $\frac{1}{2}$  m., sugar 2 oz., boiling water 20 oz.

**Potassii Borotartras** *Syn.* SOLUBLE CREAM OF TARTAR

*Dose.*—20 to 40 grains (1.2 to 2.5 g.).

Potassium acid tartrate 5, borax 2. Dissolve with heat in water, *q.s.*, and evaporate to dryness. An amorphous white powder.

**Soluble** to extent of 1 in 1 of water

Epilepsy has been treated with it—as much as 3 g. daily, sometimes combined with bromide.—*Brit. med. J. Epit.*, 1/1922, 57, *Lancet*, 1/1922, 446.—*Cl. Borax.*

Better results when combined with Gardenal than with either separately, commencing with 15 g. borotartrate and 0.15 g. Gardenal daily in three doses, continued for 3 years.—*Brit. med. J. Epit.*, 1/1929, 85.

**Sodii et Potassii Tartras** (*B.P., U.S.P. XI, P. Helv. V, P. Dan.*). *Syn.* ROCHELLE SALT, SEIGNETTE SALT, SODA TARTARATA  
 $\text{COONa} \cdot (\text{CHOH})_2 \cdot \text{COOK} \cdot 4\text{H}_2\text{O} = 282.2$ .

*Dose.*—2 to 4 drachms (8 to 16 g.).

Colourless crystals. **Soluble** 1 in 1  $\frac{1}{2}$  of water; almost insoluble in alcohol 90%.

**Pulvis Effervescens Compositus** (*B.P.*) *Syn.* SEIDLITZ POWDER, PULVIS SODÆ TARTARATÆ EFFERVESCENS.

Sodium potassium tartrate, in dry powder, 7.5 g. Sodium bicarbonate, in dry powder, 2.5 g., in the blue paper. Tartaric acid, in dry powder, 2.5 g., in the white paper.

**Pulvis Effervescens Compositus Duplex (B.P.C.)** *Syn*  
DOUBLE-STRENGTH SEIDLITZ POWDER.

Contains  $231\frac{1}{2}$  grains (15 g) of sodium potassium tartrate, double the amount in the B.P. Seidlitz Powder.

**Pulvis Effervescens Compositus Fortis (B.P.C.)** *Syn*  
EXTRA-STRONG SEIDLITZ POWDER

Contains  $173\frac{1}{2}$  grains (11.25 g) of sodium potassium tartrate, 50% more than the amount in the B.P. Seidlitz Powder

**Pulveres Effervescentes Compositi (U.S.P. XI)**

Each blue paper contains 150 gr. of a mixture of 1 part of sodium bicarbonate and 4 parts of Rochelle salt, and each white paper contains  $32\frac{1}{2}$  gr. of tartaric acid

**Citralka** (*Parke, Davis, London*) Combination of the citrates and tartrates of sodium and potassium together with salts of magnesium, calcium and lithium *Dose*—1 or 2 discs dissolved in a glassful of cold water, every 3 hours

**Salvitæ** (*American Apothecaries Co., New York, Coates & Cooper, London*) Strontium lactate 0.3, lithium carbonate 0.15, caffeine and quinine citrate 0.8, "sodu-forma-benzoas" 1.6, calcium lactophosphate 0.15, sodium and potassium citrotartrate 59.0, magnesium sulphate 8.0, sodium sulphate 30.0 *Dose*—A teaspoonful in a glass of water every 4 hours Colds and influenza

**Sodii Tartras (Neutrale).**  $(\text{CHOH}\cdot\text{COONa})_2\cdot 2\text{H}_2\text{O} = 230.06$

*Dose*—As aperient  $\frac{1}{2}$  to 1 ounce Diuretic, 15 to 60 grains repeated White crystalline powder comparatively tasteless Soluble in water 1 in 2 Relaxes the bowels and increases the flow of urine.

**Acidum Malicum.** *Syn.* HYDROXYSUCCINIC ACID.

$\text{C}_2\text{H}_3(\text{OH})(\text{COOH})_2 = 134.0$

*Dose*.—1 to 5 grains. White deliquescent crystals soluble in water 1 in 1, and in alcohol 1 in  $1\frac{1}{2}$  Has been used as throat spray in diphtheria and other throat affections. Possesses properties similar to those of tartaric acid In phthisis much larger doses—up to 2 drachms—have been given.

**DIARRHOEA, INFANTILE** Raw apple treatment, consisting of giving 1 to 4 tablespoonfuls of apple pulp every hour or two for 48 hours and nothing else to eat or drink, successful in 88% of cases—T. L. Birnberg, per *Brit med J*, 1/1933, 624

Fresh prepared apple powder better, 30 to 50 g. daily, soaked in warm water, diarrhoea completely arrested within 18 hours Not suitable for children under 9 months—P. Freud, *Brit med J Epit.*, 11/1934, 67

130 cases of acute enteritis in children from 4 months old treated with the raw apple diet with only 1 death—J. Giblin and M. Lischner, *Arch. Pediat.*, 1935, 355

## ACONITUM

*B.P., Fr Cx, U.S.P. XI, P. Helv V, F E. VIII, etc.*

[P1] "Alkaloids, the following; their salts, simple or complex—*Aconite, alkaloids of*"

[S1] "Alkaloids, the following; their salts, simple or complex—*Aconite, alkaloids of, except substances containing less than 0.02 per cent. of the alkaloids of aconite.*"

[86] "*Alkaloids—Aconite, alkaloids of—specify proportion in a preparation as the proportion of any one alkaloid of aconite that the preparation would be calculated to contain on the assumption that all the alkaloids of aconite in the preparation were that alkaloid*"

*Dose.*—No dose is given in *B P*. *Fr. Cx* has max single dose 0.1 g., max. in 24 hours 0.3 g., *FE VIII* has 0.01 g and 0.05 g respectively. *U.S.P. XI* average dose 1 grain

The dried root of *Aconitum Napellus* (Ranunculaceæ). *B P*. '32 gives no standard for alkaloidal content *B P* '14 required not less than 0.4% of ether-soluble alkaloids That of *P Belg IV*, in powder dried at 60°, contains 0.5% alkaloids, *P Helv. V* is dried at 50° and contains a minimum of 0.8% of alkaloids

*P G. V* and *Fr. Cx*—Selected heavy roots from the wild plant collected before the end of the flowering season (Not in *P G. VI*)

*U.S.P. XI* and *FE VIII* assay biologically

*Antidotes.* Empty stomach by emetic, or by using stomach tube with 180 gr. of tannic acid in 2 gallons of water Give 20 gr tannic acid in 6 oz of lukewarm water, followed by medicinal charcoal, stirred up in water Keep patient warm, and lying down with the head rather low Give 1 dr of aromatic spirit of ammonia, well diluted, every 15 minutes Strychnine,  $\frac{1}{2}$  gr, hypodermically Atropine sulphate,  $\frac{1}{100}$  gr, and digitalin,  $\frac{1}{100}$  gr, hypodermically, have been recommended Artificial respiration may be necessary over a long period Oxygen inhalations

*Uses.* Anodyne, diaphoretic, diuretic

*Externally* the liniment, as such, or mixed with chloroform or belladonna liniment in neuralgia and rheumatism (causes tingling and numbness).

*Internally* the tincture diminishes the force and rate of the pulse, especially in the early stages of fevers and mild local inflammations, such as feverish cold, laryngitis, and first stages of pneumonia and erysipelas. It also relieves the pain of neuralgia, pleurisy and aneurism Large doses cause tingling of mouth and skin generally.

Acute tonsillitis in children generally well treated by aconite For a child 5 to 10 years old, 1 to 2 minims of tincture.

Experiments on small animals show that aconite is of no avail in reducing the frequency of the pulse, but clinically good results are obtained in some manner from its use—Sir Dyce Duckworth [P1 81] **Aconitum Folium** (*B P C.*), *syn* MONKSHOOD or WOLFSBANE, consists of the dried leaves and flowering tops It contains 0.1 to 1% of alkaloids

*Fr. Cx* and *Supp* 1926 employ fresh leaves for making Alcoolature d'Aconit, 1 = 1, using 95% alcohol for macerating 8 days To contain 0.1% alkaloids. Max single dose 1 g, max. daily dose 5 g.

[P1 81] **Chloroformum Aconiti** (*B.P.C*) 1 = 1, prepared by percolating aconite moistened with ammonia with chloroform and alcohol.

**[P1 81] Collodium Anodynum (B P C.)**

Aconite about 0.1% *w/v* and veratrine about 0.7% *w/v* in acetone and acetone collodion

**[P1 81] Extractum Aconiti Radicis Alcoholicum (Fr. Cx, P Belg IV)**

Prepared from the root with 70% alcohol and standardised to 1% of alkaloids  
*Max single dose* —  $\frac{1}{2}$  grain *Max* during 24 hours  $1\frac{1}{2}$  grains approx *FE VIII* is assayed biologically *P Ital V* contains 0.5% of alkaloids

**[P1 81] Linimentum Aconiti (B P ) 1 in 2**

Prepared by percolating the root with alcohol 90% and dissolving 3% *w/v* of camphor in the percolate Useful in neuralgia *It is not suitable for painting on the gums*

**[P1 81] Linimentum Aconiti Oleosum (B P C ) Syn A B C LINIMENT**

Liniment of aconite, liniment of belladonna, liniment of chloroform equal parts To be well shaken before use, as the olive oil in the chloroform liniment is not soluble in the other ingredients *See also* Pigmentum Aconiti Compositum

The oil in the "A B C" formula seems to be essential—otherwise the preparation proves too irritant for sensitive skins

**Antidotes.** Treat as for poisoning by aconite, *see p 112*

**[P1] Mist. Aconiti (N I F )**

Tincture of aconite 1 m, tincture of belladonna 3 m, dilute hydrochloric acid 5 m, solution of mercuric chloride 10 m, water to  $\frac{1}{2}$  oz

**[P1] Pastilli Aconiti,** and **[P1] Trochisci** contain each 1 and  $\frac{1}{2}$  minims of tincture respectively Given in fevers and mild inflammatory conditions

**[P1 81] Pigmentum Aconiti Compositum (B P C )**

Liniment of aconite and liniment of belladonna, of each  $37\frac{1}{2}\%$  with chloroform and distilled water A non-oily form of A B C liniment. The water is necessary to produce a non-separable preparation

**[P1 81] Pigmentum Iodi et Aconiti (B P C )**

Equal parts of weak solution of iodine and strong tincture of aconite Used in dental periostitis Strong solution of iodine is sometimes used instead of the weak

**[P1 81] Tinctura Aconiti (B P C )**

*Dose.*—2 to 5 minims (0.12 to 0.3 ml) As a febrifuge 2 minims every 10 minutes or quarter of an hour for an hour, then repeat dose every hour till skin acts well and temperature is reduced.

Strength about 1 in 6, by percolation with alcohol 70%. It is not standardised as to alkaloidal content *B P '14* standardised to 0.04% *w/v* of ether-soluble alkaloids

*Fr Cx* is 1 in 10. It is termed *Teinture d'Aconit au dixième*, and has max. single dose 9 minims approx

*P. Ital IV, P. Belg IV* and *P Ned V* contain 0.05% of alkaloids

**[P1 81] Tinctura Aconiti (U S P XI).**

*Average dose* — 10 minims (0.6 ml)

A 10% tincture is prepared and assayed biologically, using guinea-pigs and a reference sample of aconitine It is then diluted with the menstruum and sufficient hydrochloric acid to produce a tincture of pH 3, so that the finished tincture has a potency per ml. equivalent to 0.14 to 0.16 mg of the aconitine

Aconite in small but frequent doses will often abort a quinsy. A useful prescription is—Tincture of aconite 1 m, phenazone 1 gr, caffeine citrate 5 gr, water to 1 oz To be taken every hour for eight hours—D McKenzie, *Practitioner*, 1935, 656

[P1 81] **Tinctura Aconiti Fortis (B.P.C.)**, *syn.* FLEMING'S TINCTURE OF ACONITE, is about five times the strength of the ordinary tincture. Turnbull's tincture of aconite is similar They are not used internally.

[P1 81] **Aconitina (B.P.C.)**  $C_{34}H_{47}O_{11}N = 645.4$  *Syn.* ACETYLBENZOYLACONINE.

*Dose.*— $\frac{1}{100}$  grain (0.0001 g.). Larger doses, up to  $\frac{1}{30}$  grain (0.0003 g.), are sometimes given and may be increased, if desired, with extreme caution, the maximum single dose being 0.001 g.

*Fr. Cx.* gives 0.0005 g. as maximum during 24 hours, *F E VIII*, 0.001 g, *P Helv V*, 0.0003 g

An alkaloid obtained from aconite—content about 0.3 to 0.6% of ether-soluble alkaloids, chiefly aconitine. In colourless crystals or crystalline powder, m.p. 196° to 200° when heated rapidly. A drop of dilute solution placed on the tongue produces a characteristic tingling sensation.

**Soluble** 1 in 30 of alcohol 90%, 1 in 65 of ether, 1 in 7 of benzene, and 1 in 1 of chloroform; sparingly soluble in water.

**Antidotes, vide Aconite.**

**Uses.** Employed externally (*vide* Unguentum Aconitinæ and Oleatum Aconitinæ) in neuralgia, *avoiding mucous membranes and raw skin*. Internally in the form of a pill is a depressant, calmative and diaphoretic, but rarely administered owing to extremely powerful cardiac action.

[P1 81] **Unguentum Aconitinæ (B.P.C.)**.

Aconitine 2% in oleic acid and lard. Best freshly prepared. A piece of the size of a bean is gently rubbed in for facial neuralgia, avoiding broken skin and mucous membranes.

[P1 81] **Aconitinæ Nitras.**  $C_{34}H_{47}O_{11}N.HNO_3 = 708.4$  *Dose.*— $\frac{1}{100}$  grain (0.0001 g.), hypodermically. A crystalline stable salt, soluble 1 in 10 of water and in alcohol.

[P1 81] **Granules of Aconitine** *Fr. Cx.* and of **Aconitine Nitrate** *Fr. Cx.* contain  $\frac{1}{10}$  mgr. in each, and are coloured pink.

[P1 81] **Aconitinæ Hydrobromidum**,  $C_{34}H_{47}O_{11}N.HBr.2\frac{1}{2}H_2O = 771.3$ , and

[P1 81] **Aconitinæ Hydrochloridum**,  $C_{34}H_{47}O_{11}N.HCl.3\frac{1}{2}H_2O = 735.9$ , are crystalline salts with dose as for the nitrate.

[P1 81] **Oleinatum Aconitinæ.**

Aconitine 2, oleic acid by weight 98. Dissolve; may be perfumed. Is painted on the skin (not when broken) for neuralgia.

**Bryonia (B.P.C.)**. *Syn.* VITIS ALBA, WHITE BRYONY, ENGLISH MANDRAKE.

The dried root of *B. dioica* (Cucurbitaceæ), the only species commonly found in this country—hence called English Bryony. Contains an amorphous glucosidic bitter substance and an amorphous alkaloidal principle.

**Tinctura Bryoniæ (B.P.C.)**.

*Dose.*—1 to 10 minims (0.06 to 0.6 ml.), or more. 1 in 10. Useful in pleurisy. Relieves the pain and allays the cough. In

large doses it is an active cathartic, used for dropsy. It also checks metrorrhagia. The fresh plant applied to the skin will cause vesication.

**Mandragora.** *Syn. Mandrake.* *M. Autumnalis* (Solanaceæ)

The root is often forked and is sometimes similar to the human body in shape. It is poisonous, with effects allied to those of belladonna. Contains an alkaloid. Much confusion exists over the name mandrake. The Mandrake, as pharmacists understand the Museum specimens, is to be associated with *M. officinarum* L. (this includes two varieties,  $\alpha$  *vernalis*,  $\beta$  *autumnalis* = "European" Mandrake) *English*, or false, "Mandrake" is *Bryonia dioica* *American Mandrake* is *Podophyllum peltatum*

E. M. Holmes concludes, "If Mandrake is asked for by a *herb-using* customer he should be shown *Podophyllum Peltatum*. He is not likely to ask for *Bryonia* Root under that name, and if 'Tinct. Mandrake' is asked for a doctor's script should be required"—*Pharm J*, 1/1930, 127

**Corydalis** (B.P.C.).

*Dose.*—5 to 15 grains (0.3 to 1 g.).

The dried tubers of *Dicentra canadensis* (Squirrel Corn, Turkey Corn) and of *D. Cucullaria* (Dutchman's Breeches) (Papaveraceæ). Reputed to have tonic and diuretic properties. Administered as a decoction.

**Bulbocapnine.**  $C_{19}H_{19}O_4N$ .

*Dose*— $1\frac{1}{2}$  grains (0.1 g.) either *per os* or subcutaneously once or twice daily

An alkaloid from *Corydalis tuberosa* and from *Dicentra canadensis*. Insoluble in water but soluble in alkalis, and precipitated from them by  $CO_2$  or ammonium chloride. Solutions oxidise slowly to a green colour.

Of value as a sedative in post-encephalitic conditions and in tremor of various origins—paralysis agitans, choreic disorders, multiple sclerosis, and hemiplegia.

In paralysis agitans it is better than atropine, morphine, Luminal, or scopolamine—*Prescriber*, 1929, 312

In dose as above hypodermically or *per os*, of value in the treatment of the sequelæ to epidemic encephalitis in children—*Lancet*, 1/1929, 968

Ménière's disease well treated. One tablet of 0.1 g. *per os* daily is sufficient to prevent vertigo, while the acute attack is treated by 0.1 g. hypodermically, which at once relieves—W. S. Thacker Neville, *Brit. med. J.*, 11/1931, 54

## ACRIFLAVINA

*B.P. Add.*

*Syn.* FLAVINE, ACRIFLAVINÆ HYDROCHLORIDUM (U.S.P. XI).

Acridiflavina (U.S.P. XI) is identical with euflavine

*Dose.*—5 grains have been given, but euflavine is more used *per os*

**Chemical Composition.** The B.P. '32, stated that it consists of 2 : 8-diamino-10-methylacridinium chloride hydrochloride,  $C_{14}H_{14}N_3Cl \cdot HCl = 296.1$ . It has since been shown to consist of a mixture of this compound with diaminoacridine dihydrochloride, of which it is stated by the *B.P. Add.* to contain approximately one-third

**Manufacture.** Details of the process are given by Benda (*Ber.* 45, 1787, *et seq.*) and in the patent specification. *See also* Edn., 18th, p. 313.



In the patent specification it is stated that, compared with its higher homologues, such as acridine yellow (which is 3,6-diamino-2,7-dimethylacridine hydrochloride), this body has the advantage of being very soluble, and these hitherto "unknown salts of 3,6-diamino-10-alkyl- or aralkyl-acridine have proved specifics against trypanosomes."

The trypanocidal property depends greatly on the presence of the methyl group attached to the nitrogen atom

A reddish brown crystalline powder

**Solubility.** 1 in about 3 of water (commercial samples vary considerably owing to variations in the proportions of the two constituents present), 1 in 40 of alcohol, 1 in 4 or less of glycerin. Insoluble in liquid or soft paraffin, oleic acid, and eucalyptol. The solubility of 2,8-diamino-10-methylacridinium chloride hydrochloride is 0.4% and of diamino-acridine dihydrochloride 0.6%. Mixtures of the two are more soluble. Concentrated aqueous solutions are brown, dilute ones lemon-yellow with green fluorescence

For details of the solubility in water of acriflavine and its constituents, see M. Gailliot, *Quart. J. Pharm.*, 1934, 63; also G. F. Hall and A. D. Powell, *Quart. J. Pharm.*, 1936, 510

**Compatible** with normal saline if required for immediate use, but deposits after about 24 hours. Concentrations of saline higher than 5% give a precipitate almost at once

Compatible with 0.5% sodium citrate

**Incompatible** with Dakin's solution, eusol and other chlorine antiseptics. Also with mercuric chloride solution (e.g., 1 in 1000 as used), also with phenol (e.g., 1 in 20 solution)

Solutions may be boiled or heated in an autoclave to 130°

*To remove acriflavine stains from the hands, etc.*—Rub with a little dilute hydrochloric acid or with a little dilute sulphurous acid, or with sulphurous acid followed by hydrochloric acid, and then wash with water

**Antiseptic Powers.** It is markedly antiseptic. It does not affect phagocytosis, is non-irritant, and its activity is not altered by the presence of serum. The original view (C. H. Browning and co-workers, *Brit. med. J.*, 1/1917, 73) that it was more effective in the presence of serum has been modified. The action is very slow, not less than 24 hours' contact being adopted by Browning for his experiments. It also has trypanocidal activity, but is not used in trypanosomiasis

Flavine inflicts a certain amount of damage on white blood corpuscles. It loses its power by being absorbed by muscle, dressings, etc.—Sir A. Wright, *Brit. med. J.*, 11/1930, 735.

Acriflavine is 20 times more powerful against *S. aureus* than mercuric chloride, and 800 times more so than phenol or chloramine.

**Pharmacology.** M.L.D. intravenously for dog and rabbit 30 mg. per kilo. Dogs injected intravenously at short intervals with doses from 5 to 25 mg. per kilo develop pathogenic liver and kidney changes with extensive destruction of

erythrocytes and derangement of metabolism—R S A Heathcote and A L Urquhart, *J Pharmacol*, Feb, 1930, 160

It has a stimulant action on the cat's uterus and its administration intravenously to pregnant females would appear to be contraindicated—N Sapeika, *Quart J Pharm*, 1934, 44

The **Therapeutic Coefficient** ("T.C.") of Browning is the ratio between the highest concentration of the substance, which does not reduce the phagocytic count below half that of the control, to the weakest concentration of the body which is sufficient to kill staphylococci in the presence of serum. Acriflavine and brilliant green gave the highest ratios. Acriflavine is less irritating to conjunctival epithelium than brilliant green. Both stimulate granulation in wounds.

The "T.C." of acriflavine is 200, *i.e.*, it kills both cocci and *B. coli* in concentration of 1 : 100,000, whereas to affect phagocytosis a concentration greater than 1 : 500 is requisite.

T.C. of mercuric chloride is  $\frac{10,000}{7000} = 1.4$ ; of phenol  $\frac{250}{500} = 0.5$ , and so on.

**Uses.** The dye is advised for prompt application to wounds soon after infliction, to prevent sepsis by destruction of virulent organisms before they have time to multiply, and thus to facilitate healing by first intention. Liquor Acriflavinae (equal in bactericidal effect on staphylococci to an 80% phenol solution) is a non-irritant and painless application to the surface of wounds.

A contaminated wound, within the first few hours of infliction, if thoroughly cleaned with 1 in 1000 solution—as much as possible being left in the cavity—may be sewn up and will heal by first intention. The same result may be expected in war wounds if similar facilities are permitted, but on the whole this is not favoured. It is better to pack the wound with the soaked gauze for 3 or 4 days after requisite surgical procedure. Suppuration may thus be aborted in many cases. Inject the solution into the surrounding tissues and muscle planes with a syringe and fine needle if there is extensive damage to the tissues.

Acriflavine is also advocated at the time of secondary operations to prevent the recrudescence of sepsis when operating in an area already affected.

**For suppurating wounds** the solution is used to swab out the open wound once or twice a day *after free drainage has been secured*. All the crevices of the wound are to be reached and sloughs, etc., removed. Then lightly pack with gauze steeped in the solution and cover with a "protective." Several ounces of the solution may be safely left in the tissues or peritoneal cavity. In cases showing spreading inflammatory conditions, it is well to inject the antiseptic into the part, and especially around the edges, with a hypodermic serum syringe.

When the infection has been practically overcome, weaker solutions, *e.g.*, 1 : 5000, may be used, or the treatment may be intermitted for a day every few days, dry dressing being substituted

in the intervals, or "stimulating" applications, *e.g.*, brilliant green solution 1 in 1000, may be employed.

Inlet tubes may be used, but frequent periodic flushing, *e.g.*, every 2 hours, with an aqueous solution (Carrel's method) is to be *avoided*.

Gauze steeped in the solution is specially favoured, as the dressing need only be changed once or twice in 24 hours.

The emulsion is extensively used as an antiseptic dressing for plugging suppurating wounds. It is also of value for treating burns.

The muscles round the site of an infected wound may be injected with several ounces of 1 : 1000 solution without ill effect.

**General Local Use.** Strengths ranging from 0.1 to 1% are used for the ear, skin (eczema, sycosis, folliculitis, etc.) *v. postea*. 1 in 4000 may be used in conjunctivitis and gonorrhœal ophthalmia, and 1 in 1000 is used as a urethral injection in gonorrhœa, injections being made twice daily, but for this purpose euflavine, being neutral, is preferred. A 0.5 to 1% solution in alcohol is of value in various skin diseases such as crusty eczema, pyoderma and impetigo. Four-hourly compresses of 1 in 1000 solution may be applied in pemphigus neonatorum and impetigo contagiosa.

**Intravenous Injection.** The preparation has been tried even to the amount of 300 ml of 1 in 1000 solution. The injection is given slowly—at the rate of 50 ml per minute. The method has not been largely practised. *Euflavine is preferable*.

Owing to the frequent occurrence of jaundice following intravenous acriflavine therapy, Imperial Chemical Industries Ltd, Dyestuffs Group, were asked to investigate the matter, and they have now succeeded in supplying an acriflavine (Acriflavine Intravenous) which is apparently non-toxic. Patients receiving acriflavine should always be tested for the presence of urobilinogen in the urine and the use of the drug discontinued if it is found.—E. W. Assinder, *Lancet*, 1/1936, 305.

*For references in the literature to toxic effects see 20th Edn, Vol. I*

Neither staphylococcal nor streptococcal infections are touched by acriflavine when distributed to them through the blood stream.—E. L. Walker, *J. Pharmacol.*, 26, 461.

**Subcutaneous and Intramuscular** injections of 5 to 10 ml. of 1 in 1000 solution have been given. It has been used hypodermically in lymphangitis.

### **Emulsio Acriflavinae (B.P.C.)**

Acriflavine, 1 in 1000, with liquid paraffin, white beeswax and distilled water.

*U.C.H.* has acriflavine 0.1, thymol 0.005, japan wax 3.25, liquid paraffin 76.65, water 20.

The following has also been suggested: Dissolve acriflavine 0.5 g. in warm boiled distilled water 25 ml; sterilise wool fat 30 g., put in a sterile mortar, add the solution in small portions with stirring, and finally add liquid paraffin to 500 ml.—W. J. Clarke, *Pharm. J.*, 11/1932, 435.

The emulsion in use at the City of London Hospital is prepared as follows. Acriflavine 1 g. is dissolved in distilled water 100 ml., to this is added olive oil 100 ml., oleic acid a few drops, and saccharated solution of lime about 10 ml.; triturate to form a cream and add olive oil or liquid paraffin to produce 1000 ml. This emulsion with the addition of aromatics is being used with success in the after-care of surgical cases, such as chronic empyema and lung abscesses where

there is offensive discharge and where an antiseptic deodorant dressing is indicated for plugging 3 ml. of the following aromatic essence is added to 100 ml. of the acriflavine emulsion: guaiacol 12.5 ml., oil of eucalyptus 25 ml., thymol 6.25 g., methyl salicylate 25 ml., oil of lemon to 100 ml.—W Trillwood, *Prescriber*, 1935, 293

None of the acriflavine in emulsion of acriflavine diffuses into a watery medium unless the two are briskly shaken together, a procedure which has no parallel in clinical use. It is possible that acriflavine behaves differently in contact with tissues.—L. P. Garrod, *Pharm J*, 1/1935, 324, 329

**Flavine-starch poultices** in the treatment of eczema. 4 tablespoonfuls of rice starch and 10 gr. of acriflavine mixed with cold water, 1 pint of boiling water added, and the mixture boiled till it thickens. When nearly cold pour on to dressing cloth, to form a layer  $\frac{1}{4}$  inch thick. When cold and set, cover with a layer of gauze and apply to part. Change 3 or 4 times a day and bathe part at each change with acriflavine 1 in 1000 in 0.85% NaCl. Resistant cases of seborrhoeic eczema successfully treated by this method.—*J trop Med (Hyg)*, 1923, 196

#### **Guttæ Acriflavinæ ex Alcohole (Mid H)**

Acriflavine 0.1, alcohol 90%, 50, water to 100. For otorrhœa

#### **Liquor Acriflavinæ (B P C)**

Acriflavine, 1 in 1000, in normal saline.

**Pessus Acriflavinæ (B P C)** contains  $\frac{1}{2}$  gr (0.008 g)

**Tabellæ Acriflavinæ (B P C)** contain  $\frac{1}{2}$  gr (0.03 g) in chocolate basis.

#### **References to Acriflavine.**

BURNS and pyogenic conditions well treated. No interference with granulation.—C Bennett, J W S Blacklock and C H Browning, *Brit med J*, 11/1922, 306

A 1 in 1000 emulsion in pure sterile medicinal paraffin, applied as a dressing, preferable to tannic acid. Painless and quite harmless to the conjunctiva or any mucous surface. Burns remain clean, free of septic infection and with no tendency to scarring and contraction, and no hard scab is formed as with tannic acid.—N H. Mummery, *Lancet*, 1/1933, 662.

Daily anointing with the solution produces a film, which increases in thickness and falls off in about 10 days, leaving a marvel of healing.—W Robertson, *ibid*, 830

GANGRENE, MOIST, of arm and leg, and hernia of spleen, well treated with flavine.—W J Sheehan, *Brit Med. J*, 1/1930, 822

GONOCOCCAL INFECTIONS OF THE URETHRA. Intravenous injections of acriflavine 0.3 g in 100 ml of normal saline, followed at weekly intervals by second and third injections and a week later by 0.4 g in 130 ml, were of varying activity. A special apparatus for injection is described.—*J R.N.M.S.*, Oct., 1925, 250

Acriflavine intravenously sufficient without any other treatment to cure old-standing cases of gonorrhœa. Usual course 15 injections 5 ml 2%.—Per *J Amer med Ass*, 1/1927, 211. See also R D Herrold and H Culver, *ibid*, 460

From the treatment of over 100 patients with acute gonorrhœa it was concluded that acriflavine given by deep subcutaneous injection will cause urethral discharge to disappear quickly, but relapses are common and local pain at site of injection makes it unsuitable for use in an out-patient clinic. Its use is not without danger. Jaundice is apt to appear after a long latent period and deep subcutaneous injection may lead to local pain and abscess formation. It appears to lessen the incidence of complications but has no beneficial effect when these are established.—E Hughes and C A Birch, *Lancet*, 11/1933, 634.

At the Venereal Diseases Dept. of the General Hospital, Birmingham, all cases of acute gonorrhœa are given as a routine 10 intravenous injections of 2 to 4 ml of a 2% solution of acriflavine in sterile distilled water (one injection every second or third day) with restriction of fluid to increase acriflavine concentration in the urine. This is combined with supplementary treatment such as vaccine, irrigation, and potassium citrate, 60 grains thrice daily. In the 4885 cases so treated the most noticeable feature has been the short duration of the urethral discharge which ceases as a rule in 7 to 10 days; the duration of the actual infection is also much shortened.—E. W. Assinder, *Lancet*, 1/1936, 304.

**IMPETIGO CONTAGIOSA** The 1 in 1000 emulsion in paraffin the most suitable treatment—A. R. Balmain, *Lancet*, 11/1926, 487, see also J. F. Christie, *Brit med J.*, 11/1927, 1033

**MENINGITIS** refractory to serum treatment successfully treated with doses of 5 ml of 2% solution intravenously—*Per Med Annu*, 1931, 88

**OPHTHALMIC SURGERY** Flavine 1 in 4000 can be safely dropped into the eye twice daily to prevent septic sutures—Sir A. Lawson, *Brit med J.*, 11/1927, 1129

Corneal wounds well treated—C. Killick, per *Prescriber*, 1923, 75

**OTORRHOEA** A few drops of 1% solution in distilled water, of value—S. N. Consul, *Indian med Gaz*, Aug., 1925, 374

**PERINEAL DRESSINGS** Emulsion in liquid paraffin 1 in 1000 used as a routine dressing in perineorrhaphies. The dressing renewed after each micturition. When operating for the cure of prolapse, with reasonable nursing, the wound will heal by first intention—M. A. Dobbin Crawford, *Lancet*, 11/1929, 980, *Brit. med J.*, 1/1930, 822, see also E. M. R. Fraser, *Brit med J.*, 11/1930, 1066

**PSORIASIS** Intravenously 0.1 g. in 20 ml. of water, thrice weekly, well tolerated and of benefit—*Prescriber*, 1931, 357

**PUERPERAL SEPSIS** Prophylaxis in Midwifery. One tablet (1.75 grains) in 4 ounces glycerin, previously heated to 110° and cooled, makes a 1 in 1000 solution for vaginal injection. Non-irritant and highly toxic to pathological bacteria, including the gonococcus—J. L. Moir, *Brit med J.*, 1/1931, 118, see also under Glycerin

Intravenously acriflavine would be worth trying in early cases of puerperal sepsis. Dog experiments, using 1 ml. of 1% solution per 10 lbs. weight—*Lancet*, 1/1931, 143.

**PUERPERAL SEPTICÆMIA AND PYÆMIA** "Flavine" 1 in 1000 of saline intravenously as a routine. Dose—10 to 15 ml. once a day, but in severe cases twice—B. Whitehouse, *Brit med J.*, 11/1920, 267

**RHEUMATISM** 23 out of 33 cases cured by intravenous injection of 1 ml. of 2% solution of acriflavine hydrochloride. Two injections usually gave relief from pain. Phagocytic action. No untoward effects—Norioaka, *J. Amer. med. Ass.*, 1/1929, 1022

**TUBERCULOSIS, PULMONARY** Advanced cases greatly improved following hypodermic injection of a 1 in 1000 solution of acriflavine in normal saline, the first dose being 5 minims, increased to 10 minims every 48 hours, and further to 25 minims every fourth day. As much as 40 minims twice a week given—G. H. Johnson, *Brit med J.*, 1/1926, 567 see also R. Aidin, *Brit med J.*, 11/1927, 217

**TUBERCULOSIS.** Neither acriflavine in doses up to 0.2 g., nor mercurochrome up to 0.005 g., had any recognisable effects in the treatment of tuberculous patients. A case of septicæmia, complicating ischio-rectal abscess, which had as a maximum dose 0.01 g. of acriflavine seemed to show definite improvement. 1 ml. of acriflavine 1 in 5 has been injected intravenously—G. R. Gittins, *Brit med J.*, 1/1927, 857

**UNDULANT FEVER** Cured by intravenous injections, commencing with 0.1 g. increased by 0.1 g. to 0.5 g. at increasing intervals of one, two and three days—*Brit med J. Epi*, 11/1929, 1

**Euflavina (B.P.C.).** *Syn. and Prop. Name* ACRIFLAVINA (U.S.P. XI), NEUTRAL ACRIFLAVINE, NEUROBI AVIN, 2.8-DIAMINO-METHYLACRIDINIUM CHLORIDE, TRYPAFLAVIN (*Bayer Products, London*)  $C_{14}H_{14}N_3Cl = 259.6$

*Dose.*—Internally  $\frac{1}{2}$  to 1 grain (0.03 to 0.06 g.) in tablets "enteric coated."

An orange- or brownish-red powder prepared from acriflavine by neutralisation and precipitation with sodium chloride.

This substance, being more basic than acriflavine, is even less irritant to mucous tissues and more suited for use *intravenously*.

**Soluble** in water, 1 in 4 of warm water, slightly soluble in alcohol 90%, almost insoluble in ether, chloroform and oils.

**Uses.** As for acriflavine Stronger solutions can be employed For *local use* to wounds 1 in 1000 to 1 in 500. For *bladder irrigation* and *urethral injection* 1 in 4000 to 1 in 1000. For skin infections 1% in alcohol

*Intravenously* 1 in 1000 to 1 in 200 in lymphangitis, enlarged tuberculous glands and threatened sepsis 50 to 100 ml. of this has been given 50 to 100 ml of 1 in 200 solution, in rheumatic fever, influenza, pneumonia, endocarditis, puerperal fever, septic abortion, erysipelas, etc ; 1 in 500 to 1 in 100 in gonorrhœa

Neutral acriflavine in concentrations of 1 in 100 to 1 in 1000 caused survival in guinea-pigs infected with highly virulent diphtheria bacillus It was 50 times more effective than phenol B I P P not found effective —C H Browning and R Gulbransen, *Brit med J*, 1/1925, 688

EPIDEMIC ENCEPHALITIS well treated with intravenous injections of neutral acriflavine, 8 consecutive injections of 10 ml of a 0.5% solution being given Injections given slowly at rate of 10 ml in 5 minutes —*Brit med J. Epit*, 1/1926, 34

GONORRHOEA Euflavine  $\frac{1}{2}$  grain *per os* thrice daily with mercuric oxycyanide irrigations 1 in 12,000 to 1 in 8000, renders the urine clear in the majority of cases within a week —A O Ross, *Lancet*, 11/1930, 1206

In gonorrhœa less injury to urethra if gelatin solution used instead of water or normal saline Neutral acriflavine dissolved in water to strength 1 in 4000, heat to 60° and add gelatin 10%, keep in vacuum flask One injection daily retained for 8 minutes —R D Herrold and H Culver, *J Amer med Ass*, 1/1927, 459

**Carbasus Euflavinæ (B P C)** Euflavine Gauze 0.1%.

**Tabellæ Euflavinæ (B P C.)** contain  $\frac{1}{2}$  gr. (0.03 g.) in chocolate basis

**Gonacrine** (*Pharmaceutical Specialities (May & Baker) Ltd, London*) Enteric-coated euflavine tablets

**Panflavin Tablets** (*Bayer Products, London*) contain as active principle 0.003 g of Trypaflavin *Dose*—1 or 2 to be sucked hourly as influenza prophylactic and in inflammatory and ulcerative conditions of the mouth and throat

**Planacrine** (*Pharmaceutical Specialities (May & Baker) Ltd., London*) Euflavine lozenges 3 mg flavoured with glycyrrhizin Mouth and throat disinfection

**Homoflavine** is the hydrochloride of 2.7-dimethyl-2.8-diamino-10-methylacridinium chloride Closely resembles acriflavine

**Proflavina (B P C)** *Syn* 2. 8-DIAMINOACRIDINE SULPHATE,  $C_{13}H_{11}N_3 \cdot H_2SO_4 = 307.2$

An orange-red to brownish-red powder The concentrated aqueous solution is brown It stains the skin yellow similarly to acriflavine Dilute solution is also light yellow with greenish fluorescence

**Solubility.** 1 in 300 of water, 1 in 48 of alcohol 90%, 1 in 10 or less of glycerin, insoluble in liquid paraffin, oleic acid, soft paraffin and eucalyptol

**Compatible** with normal saline solution as distinct from acriflavine (*qv*).

**Antiseptic Powers.**—This compound resembles acriflavine in being strongly bactericidal for all the common pathogenic bacteria. As weak a solution of proflavine as 1 : 200,000, it is stated, will kill *Staphylococcus aureus* in the presence of serum.

The general toxicity of proflavine for mice as tested by subcutaneous injection, and the irritating effect of concentrated solutions on the conjunctiva, are markedly less than those of acriflavine. They may be applied to the peritoneum with safety.

—C. H. Browning and co-workers.

**Uses.** Similar to those of acriflavine, but it is stated to differ in that it exerts a degree of hæmostatic action

**Proflavine Tablets.**—0.87 grain (with sodium chloride) make 2 ounces of 1 in 1000 solution, also 1.75 grains with sodium chloride to produce 4 ounces of solution

**Proflavine Bougies.** Contain  $\frac{1}{4}$  grain (0.03 g.) in oil of theobroma, 4 inches long.

**Lotio Proflavinæ (Pro Oculis).**

Proflavine 1 grain in 10 ounces

Useful in ophthalmic surgery 1 in 1000 non-irritating, but 1 in 4000 is strong enough

**Rivanol** (Bayer Products, London) is 2-ethoxy-6,9-diaminoacridine lactate

A yellow dyestuff soluble about 1 in 15 of water, incompatible with acids and normal saline and unstable in solution with Novocain and Decicain.

Used in 1 in 2000 to 1 in 500 solution as an antiseptic for wounds, puerperal infection, furunculosis and for antiseptics of the abdominal cavity. For injection for deep antiseptics requires 0.25 to 0.5% of procaine hydrochloride or 0.025 to 0.05% of Decicain. 1 in 5000 solution is given as enema in amœbic dysentery

The dye has powerful antiseptic action. Recommended in acute and chronic conjunctivitis —W. Rumbaur, per *Prescriber*, 1924, 62

**AMŒBIC DYSENTERY** Given rectally 1 in 2000 irritating 1 in 10,000 has no lethal effect on entamœba. No marked lethal action given *per os*, but may relieve colic and tenesmus —Prof. Biggam and M. A. Arafa, *Lancet*, 1/1930, 1335

**PUERPERAL SEPSIS** treated by 0.1 g. in 100 ml. water with 0.3 g. of sugar added intravenously 60 to 80 ml. given. A second injection may be needed. Drop in temperature caused and general condition improved —G. H. Morrison, *Lancet*, i/1931, 217

The sterilising concentration of acriflavine *in vitro* is lower than that required by Rivanol —C. H. Browning and R. Gulbransen, *J. Pharmacol.*, Oct., 1928, 194

**Tetraphan** (Riedel-de Haen, Berlin, Old Strand Chemical and Drug Co., London) Dihydronaphthacridinemesocarboxylic acid in tablet form. Dose — $\frac{1}{4}$  grain (0.05 g.) twice daily, increasing to  $1\frac{1}{4}$  grains (0.1 g.) twice daily if well tolerated.

In tabes dorsalis, pseudo-tabes, disseminated sclerosis, and various other nerve affections

## ADEPS LANÆ

B.P., U.S.P. XI, P. Ned. V, P. Ital. V, F.E. VIII,  
P. Dan., P. Helv. V.

Syn. ANHYDROUS LANOLIN, WOOL FAT.

The purified yellowish cholesterol fat of sheep's wool, m.p. about 40°. Sheep's wool yields from 10 to 30%.

Method of manufacture.—See *Chem. & Drugg.*, ii/1934, 179

**Soluble** 1 in 25 of ether, 1 in 18 of oil of turpentine (both with some residual matter), almost insoluble in alcohol 90%.

Adeps Lanæ can only be saponified by alcoholic solutions of potassium hydroxide under pressure—paraffin can be easily detected by this means.

**Adeps Lanæ Hydrosus (B.P.).** HYDROUS WOOL FAT

Syn. LANOLIN. Wool fat 7, distilled water 3. Melt and mix.

*U.S.P. XI, P. Dan, Fr Cx, P. Belg. IV and P. Ned V* have 25% of water *P Ital. V* has wool fat 30, liquid paraffin 6, water 10.

Yellowish white ointment basis. More water, up to about equal weights of fat and water, may be incorporated with it without affecting its consistence. Soluble partly in alcohol, while ether and chloroform dissolve only the fats it contains.

Unmixed wool fat is not readily absorbed by the skin, but when mixed with olive oil or soft paraffin absorption is much more rapid and the stickiness greatly reduced. These mixtures may be mixed with considerable proportions of aqueous liquids forming water-in-oil emulsions, the wool fat serving as the emulsifying agent. It helps absorption of narcotic extracts, quinine, iodine, potassium iodide and chaulmoogra oil.

When an ointment containing mercuric chloride or carbolic acid is ordered, it is usually intended for antiseptic purposes, therefore the *anhydrous* should be used, otherwise caustic action may result.

**BURNS.** Lanolin best application for burns. Clean the area and apply compresses soaked in a mixture of lanolin 4 and vaseline 1, kept fluid in a water-bath. At first change daily, cleaning with weak permanganate, then normal saline, followed by alcohol and ether. Dry and re-apply dressing.—*Lancet*, 11/1925, 1238.

**Unguentum Adipis Lanæ (B.P.C.)** *Syn* UNGUENTUM LANOLINI ANHYDROSI. Equal parts of wool fat and yellow soft paraffin.

**Unguentum Adipis Lanæ Compositum (B.P.C.).**

*Syn.* UNGUENTUM LANÆ COMPOSITUM, EMOLLIENT OINTMENT. Lard and wool fat, 40% of each, and yellow paraffin ointment 20%.

**Unguentum Adipis Lanæ Hydrosi (B.P.C.).** *Syn* UNGUENTUM LANOLINI. Equal parts of hydrous wool fat and yellow soft paraffin.

Similar preparations suitably perfumed form Toilet Lanolin and Lanolin Cream.

**Cholesterol.** *Syn* CHOLESTERIN  $C_{27}H_{45}OH$ ,  $H_2O$  — 404.4

Is prepared from wool fat. It is also a constituent of gall-stones, often to the extent of 90% or more, and can be obtained from these by extraction with spirit. It is a white odourless crystalline compound, m.p. about 145°.

**Soluble** in ether and hot alcohol; insoluble in water. Has been used in alopecia as a spirituous lotion,  $\frac{1}{4}$  to  $\frac{1}{2}$ %. Soft paraffin mixed with  $\frac{1}{2}$  to 1% will take up 10 to 20% of water.

**Cholesterol Metabolism.**

In **EPILEPTICS** the average blood cholesterol is subnormal and is more variable at the time of fits than in periods of freedom from attacks, a fall usually preceding an attack—M. Gosden, J. T. Fox and W. R. Brain, *Lancet*, 11/1929, 14.

**MENTAL DISORDERS** cholesterol is an important controlling factor in oxidation processes, its power being best exercised in relation to lecithin when both substances are present in normal amounts in the blood. Brains of general paralytics are remarkably deficient in cholesterol and a case of dementia præcox was completely cured by parenteral injections of 0.25 g. of cholesterol in olive oil.



every third day for a month and then  $\frac{1}{2}$  g. in emulsion by the mouth for two months, with a special cholesterol-promoting diet—B H Shaw and J. S Sharpe, *Brit med J*, 11/1931, 252

**During PREGNANCY** there is a disturbance of cholesterol metabolism resulting in large changes in the ratio of free to ester cholesterol in the plasma, but in less definite changes in the total cholesterol. There is a great increase in the percentage of plasma cholesterol (free and ester) in subacute parenchymatous nephritis, associated with an increase in the cholesterol ester content of the kidney. Some eliminate from diet in cholelithiasis all substances high in sterols, e.g., eggs, milk, butter, and suggest that diet should be restricted in this way during pregnancy—J Addyman Gardner and H Gainsborough, *Lancet*, 1/1929, 603, 619

**The photo-active function of cholesterol in skin cancer**—Prof A H Roffo, *Lancet*, 11/1931, 1187

**TUBERCULOSIS** 50 injections of 0.2 g in 5 ml olive oil, in 10 weeks, gave rapid improvement in grave anæmia and tuberculosis—*J Amer med Ass*, 1/1926, 1103

**Camphosterin** (*Richter, London*) Cholesterin 0.05 g, camphor 0.20 g, guaiacol 0.05 g, quinine 0.05 g, olive oil to 2 ml. *Dose*—2 ml intramuscularly on alternate days for a course of 20 injections. In pulmonary tuberculosis

**Oxycholesterol.**  $C_{27}H_{44}O_2$  A white unctuous substance, m.p. about 40°. Readily takes up water (up to 500%) forming water-in-oil emulsions. Is used in toilet creams

**Adeps** (*B.P., U.S.P. XI*) *Syn* ADEPS PRÆPARATUS, ADEPS SUILLUS (*P. Helv V*), AXUNGIA (*P. Ned V*), ADEPS LOTUS (*P. Dan.*)

The purified fat of the hog, *Sus scrofa* (Linn.)—from the “flare” or “omentum” which also contains 60% triolein, sold when separated by freezing and pressure as “Lard Oil,” (**Oleum Adipis**), a colourless or pale yellow oil with peculiar odour. The remainder is palmitin and stearin. **Soluble** 1 in 22 of ether, hardly soluble in alcohol. **Adeps Induratus** is for use in the tropics. The liquid constituent is removed to a great extent by pressure

**Adeps Benzoinatus** (*B.P.*), *syn* ADEPS BENZOATUS (*P. Dan.*), is made with 3% benzoin. To be avoided as a basis for eye ointments

**Adeps Benzoinatus** (*U.S.P. XI*) is made with 1% of Siam benzoin, and 5% or more of lard may be replaced by white wax in southern latitudes or in the warm season in other parts

**Sevum** (*B.P., U.S.P. XI, P. Helv V*) *Syn.* SEVUM PRÆPARATUM.

The purified internal fat of the abdomen of the sheep, prepared by cutting up the fresh omentum, melting and straining. M.p. 45° to 50°

**Soluble** 1 in 60 of ether and 1 in 45 of boiling alcohol 90%

**Sevum Benzoinum** (*B.P.C., P. Helv. V*) *Syn* SEVUM BENZOATUM. Suet digested with 3% of benzoin.

**Sevum Phosphoratum** (*B.P.C.*) Contains 10% of phosphorus

**“University Cream.”** *Syn* EMULSIO SEVI (formerly in *U.C.H.*) Beef suet 40 ozs, arachis oil 5 ozs, syrup 25 ozs, benzoic acid 40 grains, decoction of Irish moss 70 ozs, water to 1 gallon. Melt the suet, add the oil and the benzoic acid. Heat the moss decoction to about 60°, place in an emulsifier and add the fats at about the same temperature. Finally add the syrup and water. This keeps well and mixes well with milk. For use instead of cows' cream in preparing infants' feeds

"New Zealand Cream" as manufactured in New Zealand's Government factory and intended for use throughout that country, contains 50% fat, of which  $\frac{1}{2}$  is animal oil, including fresh New Zealand butter and cod-liver oil, and  $\frac{1}{2}$  vegetable oils, mainly pea-nut, sugars, mainly dextrose and a little lactose, make up 40%. Satisfactory in use, readily assimilable, sterile, containing vitamins intact, and high caloric value of 180 per ounce—R Jewesbury, *Brit med J*, 1/1926, 245 See also p 345

## ADRENALINA

B P., P. Belg. IV, Fr Cx, P Ned V, P. Ital. V



*Syn. and Prop Names* ADRENALIN, HEMISINE, SUPRARENALIN (Armour, London), ADRENINE, RENAGLANDIN (Oppenheimer, London), SUPRARENIN (P G VI), TAKAMINA (F E VIII), ADNEPHRIN, PARANEPHRIN (Merck, Darmstadt; Martindale, London), VASO-CONSTRICTINE (Duncan, Flockhart, Edinburgh), LEVORENINUM (P Belg IV), EPINEPHRINA (U S P XI), *o*-DIOXYPHENYLETHANOL-METHYLAMINE, 1- $\alpha$ -3 4-DIHYDROXYPHENYL- $\beta$ -METHYLAMINO-ETHANOL.

[P1] "Suprarenal gland, the active principles of, their salts"

[86] "Suprarenal gland, the active principles of, their salts—specify proportion in a preparation either

- (a) as the proportion of suprarenal gland or of the cortex or of the medulla of the gland, as the case may be, contained in the preparation; or
- (b) as the amount of suprarenal gland, or of the cortex or of the medulla of the gland, as the case may be, from which a specified quantity of the preparation was obtained, together with an indication whether the amount relates to fresh or to dried gland substance"

Dose—By injection,  $\frac{1}{1000}$  to  $\frac{1}{200}$  grain (0.0001 to 0.0005 g.).

U S P XI average dose  $\frac{1}{200}$  grain

It is an active principle of the suprarenal gland first prepared by Takamine, and may be obtained from the glands or prepared synthetically (*vide infra*). It occurs as a white or pale buff-coloured crystalline powder. It appears to maintain a proper degree of contraction of the arteries and hence to correct blood pressure.

**Soluble** sparingly in water, readily in mineral acids and boric acid solution forming corresponding salts, also in solutions of sodium or potassium hydroxide. Aqueous solutions of its salts are laevorotatory. **Insoluble** in alcohol, ether, chloroform, light petroleum, liquid paraffin and other organic solvents. Oleic acid is a poor solvent. Not precipitated by ordinary alkaloidal reagents. It is chemically a powerful reducing agent.

On heating above its melting-point (263°) it decomposes with an odour resembling opium smoke—Fr. Cx B P. states m.p. 205° to 212° with partial decomposition.

**Prescribing Note.** It is best prescribed as *Liquor Adrenalinae Hydrochloridi* or other preparation given below, since it oxidises rapidly, especially in neutral or alkaline solution.

**Manufacture.** The suprarenal glands are reduced to pulp and macerated, excluding oxygen as much as possible, in warm (50° to 80°) water or very dilute acid for 5 hours, the mixture being then heated at 90° to 95° to coagulate albuminoids. This aqueous extractive is evaporated and extracted with alcohol. Precipitation from this liquid of impure adrenaline follows by means of ammonia. It is purified by ether-alcohol, and reprecipitation with ammonia or fixed alkali.

Synthetic adrenaline may be obtained by the interaction of catechol and chloroacetyl chloride to give chloroacetylcatechol which is treated with methylamine and the product reduced to give racemic adrenaline. The *lævo* compound is separated by fractional crystallisation of the *d*-tartrates. *d*-Adrenaline has only about one-fifteenth the activity of the *l*-compound and the racemic form has therefore only about one-half the activity of *l*-adrenaline.

[P1] **Liquor Adrenalinae Hydrochloridi (B.P.)**

Adrenaline 1, chlorbutol 5, sodium chloride 9, dilute hydrochloric acid 3, distilled water to 1000.

**Dose**—By subcutaneous injection, 2 to 8 minims (0.12 to 0.5 ml.). The B.P. has no dose for oral administration, but doses of 10 to 30 minims (0.6 to 2 ml.) are often given.

[P1] **Liquor Epinephrinae Hydrochloridi (U.S.P. XI)**

**Average dose.**—8 minims (0.5 ml.) by parenteral injection.

A physiologically standardised solution of adrenaline hydrochloride in water and hydrochloric acid of the same strength as *Liquor Adrenalinae Hydrochloridi*, B.P. Not more than 0.5% of chlorbutol or other suitable preservative may be added, but the nature and amount of the preservative must be stated on the label.

**Dilutions for use.** As a spray the solution is diluted to 1 in 2500, or even 1 in 5000 parts is effective in the nostrils or within the uterus.

**COLORATION OF SOLUTIONS** It is best prescribed alone. The solution is liable to become brown in colour on exposure. Oxidising agents, e.g., hydrogen peroxide, produce this effect on neutralising. Loss of activity is proportional to this coloration. A small quantity of formalin or of sodium thiosulphate retards the coloration of adrenaline solutions. Adrenaline is rendered inactive in a few hours in contact with colloidal and organic silver compounds.—*Per Prescriber*, 1927, 188.

**Possible Dangers.** Adrenaline should not be injected in chloroform anaesthesia.

**ADRENALINE IDIOSYNCRASY** Some people show toxic effects with a small dose of adrenaline, especially when it is given simultaneously with certain local anaesthetics, e.g., procaine. In dental practice this could be eliminated by avoiding the use of solutions stronger than 1/100,000. Surgeons should avoid the use of adrenaline by using a general anaesthetic, when it is found by a small preliminary injection that idiosyncrasy exists. Its use is contraindicated when operating on patients with Graves' disease.—H. E. Symes-Thompson, *Lancet*, 1/1924, 745.

Tetany following the use of cocaine and adrenaline (1 in 1000) is of fairly frequent occurrence. It is not a drug intoxication, but is due to a combination of hypoparathyroidism, hyperventilation, and epinephrin in nervous patients. Quickly relieved by parathyroid extract subcutaneously.—S. E. Roberts, *J. Amer. med. Ass.*, 11/1929, 906.

Latent and finally active tetany in a patient who received adrenaline during asthmatic attacks is considered to be the result of an alkalosis due to hyperventilation. Tetany did not appear when codeine was given in place of adrenaline. Suggested it might be advisable to test for latent tetany in asthmatic attacks.—Ellsworth and Sherman, *J. Amer. med. Ass.*, 1/1936, 284.

Alarming collapse with feeble pulse after 20 minims of adrenaline solution hypodermically repeated every two hours for six doses, improved rapidly on use of amyl nitrite.—F. R. Sawdon, *Brit. med. J.*, 11/1922, 866.

Intravenous injection of adrenaline 40 times more dangerous than subcutaneous.—*Lancet*, 1/1924, 744.

With long use there is risk of arteriosclerosis.—*Brit. med. J. Epit.*, 1/1926, 16.

Adrenaline intravenously inhibits uterine contraction before delivery. The administration of ether has a similar effect.—A. Bourne and J. H. Burn, *Pharm. J.*, 11/1927, 490.

**Uses.** When applied locally adrenaline causes constriction of blood vessels and blanching of the skin and mucous membrane. This local constricting effect lasts from  $\frac{1}{2}$  to 2 hours. It is useful for checking capillary bleeding, epistaxis and menorrhagia, the bleeding after tooth extractions, from superficial wounds and abrasions, and during operations to check hæmorrhage and blanch the parts, especially for operations on the eye, ear, nose, throat or larynx. Solutions are useful for application to the nasal mucous membrane in coryza, asthma and hay fever. Hypodermic injections are used to relieve asthmatic spasms, to control anaphylaxis from serum injection and to reduce the swelling in giant urticaria. Hypodermic injection does not materially raise blood pressure, as the local vascular constriction prevents absorption. Intravenously it is successful in surgical shock, and circulatory failure. It may be given by mouth to check hæmorrhage from the stomach, or may be injected into the rectum, bladder and uterus for bleeding. When given orally, however, it is thought by many to be destroyed by the gastric juice. It is of no value in hæmoptysis, and of little use in remote hæmorrhage however given, in fact the rise in blood pressure may increase the hæmorrhage. Intracardiac injection of adrenaline solution is employed for resuscitation in cases of heart failure and collapse under anæsthesia. Given *per os* in small doses it does not increase blood pressure unless there is suprarenal insufficiency. Adrenaline is added to local anæsthetic solutions to retard diffusion and produce ischæmia. In nose operations submucous injection of a 1 in 10,000 solution with 5 minims of 1% cocaine hydrochloride is utilised to lessen blood flow.

**ACTION ON THE HEART.** Injections of adrenaline are followed at first by an acceleration in the pulse rate and a simultaneous contraction of the muscular coat of the peripheral arteries. This causes an immediate rise in blood pressure and excites the cerebral vagus centre, which in turn slows the heart beat and strengthens the cardiac contractions. Apart from this indirect vagus action, adrenaline stimulates the heart directly. Excessive doses overstimulate the cardiac muscles and predispose the heart to fibrillary contractions.

**INTRACARDIAC INJECTION IN RESUSCITATION.** Adrenaline has been given by direct injection into the heart to revive its action when in sudden failure. It is not necessary or advisable to give

more than 1 mg. of adrenaline, *i.e.*, 1 ml. of the 1 : 1000 solution, in view of the possible danger of a tetanic contraction of the muscle with systolic stoppage of the heart. The injection may be made with a thin needle 8 cm in length. The site of puncture should vary with the form and size of the thorax and of the heart, and with the position of the diaphragm; in order to reach the left ventricle the puncture should usually be made through the fourth inter-costal space on the left sternal border. The danger zones to be avoided are the upper two-thirds of the anterior longitudinal sulcus, the atrio-ventricular septa, the bundle of His, the region of the coronary vessels and the internal mammary artery.

For resuscitation in cardiac arrest, artificial respiration should be resorted to first by the usual methods. If at the end of 3 or 4 minutes no pulse can be felt, and especially if no heart beats can be heard on auscultation, adrenaline should be injected into an external jugular vein. The abdomen should be opened high up, one hand inserted in the opening, passed up over the left lobe of the liver and the heart massaged intermittently—J A Gunn, *Brit med J*, 1/1921, 9. See also Walker, *ibid*, 4, 6, and J P Lockhart-Mummery, *ibid*, 100. (According to the last authority it was possible to revive a cat 20 minutes after all signs of life had ceased. In use it was found more effective to inject a 1 in 50,000 solution of adrenaline intravenously than to inject into the heart.)

When used for resuscitation, it is necessary to establish temporarily an artificial circulation to carry the drug to the periphery. It acts on the peripheral vessels, chiefly the peripheral arterioles, hence the intravenous injection is necessary in 2 parts or more, and in dilution of about 1 in 50,000—J P Lockhart-Mummery, *Brit med J*, 1/1921, 582.

Of 34 cases quoted in the literature of cessation of heart's action during anaesthesia treated by intracardiac injection of adrenaline, 60% have survived. Useless after 5 minutes—*Prescriber*, 1926, 141. See also E G Stuart, *Lancet*, 11/1925, 1208.

Stillborn infants responded to adrenaline by intracardiac injection—M G Cardwell, *Brit med J*, 11/1926, 638.

A warning is issued against the incautious use of intracardiac injections in chloroform syncope, since it enhances the already existing irritation of the parasympathetic. For the first injection no more than 4 minims of the 1 in 1000 solution in warm saline should be used, repeated or increased to 8 minims later—*Pr med*, 1926, 84, per *Prescriber*, 1927, 65.

The injection might damage the myocardium—Sir F Shipway, *Lancet*, 11/1931, 797. Not considered likely by Prof Gunn and Sir E Sharpev-Schafer. Cardiac massage thought preferable.

#### BACTERICIDAL PROPERTIES

Solution of adrenaline hydrochloride and aqueous extracts of the adrenals, especially the medulla, acquire marked bactericidal properties when exposed to the air—probably due to partially oxidised adrenaline. The action is most marked towards *C. diphtheriae* and *V. cholerae*, less marked towards *B. anthracis*, *Staph aureus*, *Staph albus* and *B. paratyphosus*—J. Gordon and J C Knox, *J. Path Bact*, 1934, 609.

The soluble toxins of diphtheria and tetanus can be rendered harmless by contact with adrenaline, which does not appear to affect the growth of these organisms although it renders the pneumococcus innocuous.—A C Marie, per *Prescriber*, 1935, 159.

#### References to Adrenaline.

**ALOPECIA.** Following a history of scarlet fever, fright and malaria—well treated by injection and dried thyroid *per os*—*Prescriber*, 1924, 207.

**ASTHMA.** 1 to 5 minims hypodermically gives prompt relief. Continued daily use has no harmful effect—G R Murray, *Clin J*, Aug, 1923, 363.

Many cases get relief from an injection—T Drummond, *Brit. med. J*, 1/1923, 320.

In status asthmaticus the continuous injection of adrenaline in small quantities, up to even a drachm in  $\frac{1}{2}$  hour, the only cure—A F Hurst, *Brit. med J*, 11/1929, 297.

Status asthmaticus can always be arrested by the continuous method of injecting adrenaline. The needle is kept in position, and with a full syringe and after an initial injection of a dose known to cause no unpleasant symptoms, one or more minims is injected every 15, 30 or 60 seconds (according to the patient's reaction), the rate being varied until it is found how frequently a dose can be given without causing unpleasant symptoms. The injections are continued if necessary for 30 minutes or more. Relief always follows and generally the patient falls into a deep sleep.—A F Hurst, *Pharm J.*, ii/1934, 705.

The predisposing cause of asthma is a low content of adrenaline in the blood; patients with asthma become unable to dilate the bronchiolar airway when chronic infections cause a constriction.—J H Burn, *Proc R Soc Med*, 1933, 31.

Chemical factors in the control of the circulation—adrenaline, vasopressin, histamine, acetylcholine.—H H Dale, *Lancet*, i/1929, 1179, 1233, 1285.

COLLAPSE has been treated by 0.5 to 1 ml injections every 1 to 2 hours. Intravenous injections of saline with 6 to 8 drops of adrenaline solution to the litre, are practised, also in chloroform syncope and other forms of heart failure.

FRACTURES treated by adrenaline solution 10 drops and calcium phosphate 0.1 g. twice daily, in addition to usual treatment.—*Prescriber*, 1924, 206.

GAS GANGRENE—Epinephrine, 0.5 ml, injected in vein at elbow, saved a case apparently moribund.—*Per J Amer med Ass*, ii/1925, 1435.

URTICARIAL ERUPTION successfully treated by 10 minims adrenaline hypodermically.—J R Keith, *Brit med J*, ii/1925, 1005.

HEMOPHYTOSIS—Adrenaline cannot be justified on experimental grounds, but given intratracheally over back of the tongue said to be effective (1 ml of 1 in 1000 solution in 2 ml of water.—*Munch med Wschr*, Feb, 1928), but this should not be done in an emergency when blood is welling up into the mouth. Semi-sitting posture best.—F G Chandler, *Lancet*, i/1930, 589.

HEADACHE—Headache due to obstruction of frontal sinuses. Adrenaline hydrochloride 1 in 4000, 1 dr, and saturated boric acid solution 1 dr used in an atomiser four times daily gives relief.—E Podolsky, *Int J Med*, July, 1930.

HEART BLOCK—Twelve cases of complete heart block tested with adrenaline chloride. The response of the heart is determined not by the amount of the dose but by the rate of the heart at the time of injection. High initial rates are followed by little or no gain in rate, but slow initial rates are followed by pronounced acceleration. For a given initial rate 0.25 ml of adrenaline chloride solution produced as much acceleration as a dose four times as large.—A R Gilchrist, *Quart J Med*, Oct, 1933, 483.

Rheumatic heart block well treated with adrenaline solution, 4 m hypodermically—a total of 32 m in 5 days.—G A Sutherland, *Prescriber*, 1926, 199.

MALARIAL SPLENOMEGALY well treated by means of adrenaline intravenously, starting with 0.01 mg in distilled water and increasing by 0.01 mg to 0.1 or even 0.2 mg if well tolerated, and repeat this dose for some 20 days till the splenic enlargement disappears or is no longer undergoing reduction. Blood pressure is improved and may even become normal.—P Riolo, *per Trop Dis Bull.*, 1936, 276.

MIGRAINE—Adrenaline subcutaneously aborts migraine attacks in a high proportion of cases.—T C Hunt, *Lancet*, ii/1933, 285.

PERTUSSIS—Children have taken 1 to 3 drops *per os*, or less according to age, every 3 or 4 hours with good effect.

POST-ANÆSTHETIC VOMITING checked by 5 to 8 minims of adrenaline hydrochloride solution *per os*.—V. Macdonald, *per Prescriber*, 1923, 5.

PYLORIC STENOSIS—Adrenaline intramuscularly in the forearm has decidedly beneficial effect. Given 10 minutes before feed in  $\frac{1}{2}$  mg doses as 1 in 1000 solution from 3 to 5 times daily. Good results in some cases when combined with use of atropine.—J L. Meagher, *Brit med J.*, i/1926, 89.

SERUM SICKNESS—Recovery in a case of severe serum shock in a girl of 8 years, which developed three minutes after intramuscular injection of 5 ml. of concentrated scarlet fever antitoxin, treated by artificial respiration and hypodermic injection of adrenaline hydrochloride solution.—J. Grant and M M. Scott, *Lancet*, ii/1934, 80.

STOKES-ADAMS ATTACKS well treated with adrenaline solution (5 m. doses) subcutaneously.—A G Phear and J Parkinson, *Lancet*, i/1922, 933.

Stokes-Adams attacks due to heart block following severe form of faucial diphtheria treated by frequent subcutaneous injections of adrenaline. Heart made a good recovery but patient eventually died from diaphragmatic paralysis —J. V. Bates, *Brit med J.*, 1/1934, 619

VERTIGO.—A lasting cure was obtained by giving 20 drops *per os* a day.—*Per Practitioner*, 11/1923, 232.

VOMITING IN MALARIA well treated with 7 to 8 minims—one dose sufficient —E. Lomax Wood, *per J. trop. Med. (Hyg)*, 1922, 248

X-RAY SICKNESS—A method for controlling this condition far superior to all others is the administration by the mouth of 10 minims of Liq Adrenalin. Hydrochlor as frequently as necessary up to 6 doses or even more, in the 24 hours —N. S. Finzi, *Brit med J.*, 11/1935, 1072

[D-P1 81] **Adrenaline Catheter Lubricant.**—Adrenaline (base) 1, cocaine 10, atropine 10. Dissolve the adrenaline in hydrochloric acid *q s.* (0.6 is usually sufficient) diluted with dehydrated alcohol 30. Dissolve the alkaloidal bases in oleic acid 20 and mix this and the adrenaline solution with sufficient castor oil and dehydrated alcohol in proportion of 4 to 1 to make 1000 of the lubricant.

[P1] **Guttæ Adrenalini cum Acid. Boric.** (R L O H)

Solution of adrenaline hydrochloride 1 dr, boric acid 10 gr, sterile water to 1 oz

[P1] **Guttæ Zinc. Sulph. cum Adrenalin.** (R L O H)

Solution of adrenaline hydrochloride 1 dr, zinc sulphate  $\frac{1}{2}$  to 2 gr, boric acid 10 gr, sterile water to 1 oz.

[P1] **Insufflatio Adrenalinae** (B.P.C.) *Syn* ADRENALINE SNUFF

Adrenaline, about 1 in 1300, with boric acid, camphor, menthol, potassium chlorate, oil of eucalyptus and lycopodium.

[P1] **Nebula Adrenalinae Aromatica** (B.P.C.) *Syn* ADRENALINE INHALANT

Adrenaline, 1 in 1000, eucalyptol and oil of sweet birch in an oily base.

[P1] **Neb. Adrenal. c. Benzamin. Hydrochlor.** (N I F)

Solution of adrenaline hydrochloride  $1\frac{1}{2}$  dr, benzamine hydrochloride 5 gr, glycerin 40 m, distilled water to 1 oz

[D-P1 81] **Nebula Adrenalinae et Cocainæ** (B.P.C.)

Adrenaline 1 in 5000, and cocaine hydrochloride 1% with chlorbutol and sodium chloride in water.

[P1] **Solutio Adrenalini Composita** (St T H.)

Solution of adrenaline hydrochloride 5 m, atropine sulphate  $\frac{1}{100}$  gr, strychnine hydrochloride  $\frac{1}{100}$  gr., distilled water to 10 m.

[P1] **Suppositorium Adrenalinae** (B.P.C.) contains  $\frac{1}{10}$  gr. of adrenaline.

[D-P1 81] **Suppositorium Adrenalinae et Cocainæ** (B.P.C.) contains  $\frac{1}{10}$  gr. of adrenaline and  $\frac{1}{2}$  gr. of cocaine hydrochloride

[P1] **Unguentum Adrenalinae** (B.P.C.)

Adrenaline 0.1% in a hydrous wool fat and white soft paraffin basis.

[D-P1 81] **Unguentum Adrenalinae et Cocainæ** (B.P.C.) is the same with addition of 1% of cocaine hydrochloride.

[P1] **Adrenalin Chloride Solution** (1%). (*Parke, Davis, London*).

An aqueous solution for deep oral inhalation in the treatment of asthma

[P1] **Adrenalin Inhalant** (*Parke, Davis, London*) A 1 in 1000 solution of adrenaline with 5% of chloretone in an aromatised oil Soothing and astringent in inflammatory affections

[P1 87] **Adrepatine** (*Anglo-French Drug Co., London*) Suprarenal extract, pituitary extract (total), thyroid, prostate and hepatic extracts, with stovaine and vegetable extracts—cypress, horse-chestnut and hamamelis Suppositories and ointment for treatment of hæmorrhoids

[P1 87] **Asthmolysin** (*Dr Kade, Berlin, C Zimmerman, London*) Solution of suprarenal and pituitary glands for subcutaneous injection in asthma.

[P1 87] **Bronchovydrin** (*R & O Weil, Frankfurt, Rudolph-Riddel, London*) Solution containing papaverine atropine methylnitrate, adrenaline, pituitary extract and nitrates for use as a spray in asthma and hay fever

**Cobefrin** (*Bayer Products, London*) *o*-Dioxyphenylpropanolamine Closely related chemically to adrenaline Dissolves readily in water, forming a colourless solution with almost neutral reaction The solution is much more stable than that of adrenaline, but is highly sensitive to free alkali and should not be subjected to prolonged boiling or careless exposure to light—solutions of a yellowish or brownish colour should not be used Exerts the vasoconstrictor action of adrenaline without its disturbing deleterious action on the circulation, a sudden decrease in blood pressure following vagus reflex cannot occur *Dose*—When used in infiltration and conduction anæsthesia, as many drops of a 1% solution are added to the anæsthetic solution as one usually adds of the 1/1000 adrenaline solution A maximum quantity of 15 mg (30 drops) should not be exceeded For surface anæsthesia, 1 to 10 drops are added to 1 ml of anæsthetic. It is supplied in 1% solution or combined with Novocain in tablets and solutions of various strengths

**Epinine** (*Burroughs Wellcome, London*) 3-4 Dihydroxyphenylethyl-methylamine  $C_8H_9(OH)_2CH_2CH_2NHCH_3$ , - 1671

A 1 in 100 solution equals a 1 in 1000 solution of adrenaline Solutions acidified by the addition of 0.5 ml of sulphurous acid to 100 ml are more stable than adrenaline solutions

It is supplied in 1% solution to be diluted with normal saline It resembles adrenaline in action, but the rise of blood pressure though not so intense is said to be more prolonged For use in ophthalmic work 0.1%, as a styptic to bleeding surfaces 0.01 to 1%, and hypodermically 1% solutions are used For intravenous use 1 ml of 1% solution is diluted with 500 ml of normal saline

[P1 87] **Evatmine** (*British Organotherapy Co., London*) Adrenaline and pituitary extract in 1 ml ampoules for subcutaneous injection in the treatment of asthma

**Glaucosan** (*Wölm, Spangenberg, Saccharin Corporation, London*) Solution containing 0.2% of synthetic *d*-adrenaline and 1% of methylaminoacetatechol (adrenalone) Given by subconjunctival injection in the treatment of glaucoma

[P1] **Lævo-Glaucosan** (*Wölm, Spangenberg, Saccharin Corporation, London*)

A solution containing 2% each of synthetic *l*-adrenaline and methylaminoacetatechol (adrenalone) A powerful miotic for instillation, following the use of a local anæsthetic such as Holocain 1-2%, in the treatment of chronic glaucoma The preparation must not be injected in any manner

**Amino-Glaucosan** (*Wölm, Spangenberg, Saccharin Corporation, London*) A 10% solution of histamine hydrochloride for use as a powerful miotic in acute glaucoma

Neither Lævo-Glaucosan nor Amino-Glaucosan have any prolonged effect in lowering intraocular tension, and their action is neither uniform nor dramatic The dilatation of the pupil by Lævo-Glaucosan is useful as a diagnostic as it does not raise tension; in secondary glaucoma it ruptures synechiæ Amino-Glaucosan is an extremely potent miotic—occasionally a useful adjunct to eserine Both Lævo- and Amino-Glaucosan cause severe reaction and pain and are not without danger to the cornea—W S Duke-Elder and F W Law, *Brit med J*, 1/1929, 590

Similar reports by American workers—*Prescriber*, 1929, 386

[P1 87] **Infundrenalin** (*Evans, Sons, Lescher & Webb, Liverpool*) Infundibulin 0.5 ml, adrenaline (1 in 1500) 0.5 ml (in two separate ampoules). In bronchial asthma and hay fever.



[P1 87] **Pitrenalin** (*Parke, Davis, London*) Pituitrin and adrenaline hydrochloride solution in twin ampoules producing, when mixed, a solution containing 5 i.u. of pituitary (posterior lobe) extract and 6 m. of adrenaline hydrochloride solution in normal saline to 1 ml. *Dose*— $\frac{1}{2}$  to 1 ml. hypodermically

[P1 81] **Tonolysin** (*Richter, London*) Separate ampoules of adrenaline  $\frac{1}{4}$  gr. and papaverine  $\frac{1}{2}$  gr. for subcutaneous or intramuscular injection in bronchial asthma

[P1] **Vernol Ointment** (*Allen & Hanburys, London*) Contains adrenaline 1 in 5000 with anæsthesine 1 in 40. Soothing and astringent for catarrhal conditions of the nasal mucous membrane

### [P1] **Suprarenal (or Adrenal) Gland.**

Small, flattened, yellowish bodies—one at upper end of each kidney. In man each gland weighs about 4 grammes. Each suprarenal gland is enclosed in a fibrous capsule and is composed of two parts, a cortex and a medulla. The cortex contains a glandular epithelium embedded in a fine network of connective tissue; the medulla contains finely granular chromaphil cells permeated by large venous sinusoids. These granular cells stain green with ferric chloride and brown with chromic acid.

### [P1] **Suprarenalum (B.P.C.)**

*Dose*.—1 to 5 grains (0.06 to 0.3 g.) three times a day

The cleaned, dried and powdered suprarenal glands of oxen or other mammals. An average sheep's gland weighs about 30 grains (2 g.) and yields about 5 grains of dry powder.

The powdered desiccated gland may be identified by its numerous stellate or irregularly shaped chromaffin cells which stain brown with chromic acid solution, together with its characteristic cortical cells seen in preparations stained with hæmatoxylin and eosin.—H. W. Youngken, *J. Amer. pharm. Ass.*, 1936, 103.

By glycerin extraction of adrenal glands a pressor principle effective orally can be obtained. It is believed to differ from adrenaline.—Hoskins & Gottlieb, *Endocrinology*, 1936, 21, 188.

**Uses.** Originally the fresh glands were used in the treatment of Addison's disease, later the dried glands were used, also liquid extracts and, lastly, an extract prepared from the cortex of this gland is now used in this disease. The active principle of the medulla is adrenaline (*vide antea*). The whole gland has also been used in the treatment of Graves' disease.

Raw adrenal gland of value in post-influenzal debility— $\frac{1}{2}$  gland three daily on an empty stomach. Also of value in preventing attacks of asthma.—L. J. Picton, *Brit. med. J.*, 1/1927, 641.

### [P1] **Suprarenal Snuff**

Dry suprarenal gland 1, menthol 2, ammonium chloride 6, boric acid 4, lycopodium 4, for use in hay fever.

[P1 87] **Tab. Adreno-Spermin Co.** (*Endocrines Ltd., Watford*) Tablets contain total adrenal, thyroid, spermin extract (from gonads), and calcium glycerophosphate. Also supplied in ampoules for injection. Asthenic conditions.

### [P1] **Extractum Suprarenali Corticis (B.P.C.)** *Syn* CORTIN

*Dose*.— $1\frac{1}{2}$  to  $2\frac{1}{2}$  drachms (5 to 10 ml.).

An aqueous solution of the active principle, or principles, of suprarenal cortex obtained by extraction with alcohol and subsequent purification with benzene, acetone and light petroleum.

The hormone, cortin, has now been isolated in a pure crystalline condition, free from traces of adrenaline. The crystals appear to have the formula  $C_{30}H_{50}O_8$  and its properties point to its being an  $\alpha$ -hydroxyaldehyde existing in two forms: a monomolecular form soluble in water and having aldehydic properties, and a polymeric form insoluble in water and not possessing aldehydic properties. Both forms appear to have the same physiological activity and will keep suprarenalectomised animals in normal condition—E C Kendall and co-workers (Mayo Clinic), per *Brit med J*, 11/1934, 363.

**PHYSIOLOGY** The cortex of the suprarenal gland is essential to life, it is possible to remove the medulla without causing death if the cortex is left intact. Although the exact physiology of the cortex has yet to be determined, it is known that injections of an extract relieve the symptoms of Addison's disease. The preparation of an active extract was first described by Swingle and Pfiffner (1930), who consider that the function of the cortex hormone is to regulate the volume of the circulating fluid within the vascular system. They consider that the death of animals after removal of the suprarenal glands is due to circulatory collapse resulting from insufficient circulating fluid, and suggest that suprarenal cortex extract should be of value in the treatment of traumatic shock which shows some resemblance to the condition seen in adrenalectomised animals—*Science*, 1/1933, 58.

The relationship of the suprarenal cortex hormone to sodium and chloride metabolism has been much discussed. It appears that early in the course of adrenal insufficiency the rate of sodium excretion through the kidney increases and the concentration of sodium ions in the blood decreases. There is also a decrease of chloride or of bicarbonate or of both. The loss of sodium from the body is accompanied by a loss of water which leads to decreased blood volume and a state of shock, and to a rise in serum potassium.

The relationship of the adrenal cortex to sex investigated by injections of cortical extract into normal and castrated rats. Results completely negative.—S L Simpson, A Koln-Speyer and V. Koronchewsky, *Lancet*, 11/1933, 1194.

Excess of the cortical hormone seems to have no influence on the size of the gonads, the oestrous cycle or the course of gestation in the rat. No evidence of more than one hormone in the cortex—E Howard and A Grollman, *Amer J Physiol*, Feb., 1934, 480.

The adrenal cortex has a regulating effect on the metabolism of water and of electrolytes—R L Zwemer, *Endocrinology*, 1934, 161.

The adrenal cortex—an account of the functions of the cortical hormone, its preparation and assay—R F Loeb, *J Amer med Ass*, 1/1935, 2177.

Adrenal cortex is necessary for conversion of protein to sugar, investigation of glycogen formation in liver and of urinary nitrogenous excretion in normal and adrenalectomised rats—G Evans, *Amer J Physiol*, 1936, 111, 297.

The occurrence of vitamin C in the suprarenal gland is referred to in *Vol II* (20th Edn.), page 383. It is present in considerable quantities in the cortex and to a less degree in the medulla. Whether the gland merely serves as a reserve storage organ or requires the vitamin for its own normal functioning is still a matter of controversy.

**Uses.** Suprarenal cortex extract is employed in the treatment of Addison's disease. It has also been used to some extent in neurasthenia, glaucoma and in the persistent vomiting of pregnancy.

For use of sodium chloride in Addison's disease, see under Sodium Chloridum.

**ADDISON'S DISEASE**—Chief value of cortical extract in Addison's disease is in treatment of the relapse, the extract has no definite effect on hypotension or pigmentation—G. A. Harrop and others, *J. Amer. med. Ass.*, 1/1933, 1850.

Oral therapy with suprarenal cortex extract effective in Addison's disease if dose is 3 to 5 times larger—H. S. Stannus, *Brit. med. J.*, 11/1933, 1112.

If adrenal insufficiency is not relieved by sodium chloride it will not respond to commercial adrenal extracts given in the usual dosage—R. F. Loeb, *J. Amer. med. Ass.*, 1/1935, 2130.

Treatment of Addison's disease with 3 g daily of minced and dried fresh adrenal tissue deprived of fat—C. S. Hicks and M. L. Mitchell, *Proc. R. Soc. Med.*, 1935, 28, 932.

**BURNS, ACUTE TOXÆMIA OF**—In severe toxæmia death within 100 hours is the usual outcome, whatever the treatment, but three such cases in which a fatal outcome was to be expected recovered following the use, as an adjuvant measure, of extract of suprarenal cortex (Eucortone). A dose of 1 ml subcutaneously every two hours from the onset of acute toxæmia will suffice for a child, and 2 ml or more every hour for an adult, injections should be continued till 100 hours after injury and renewed if toxic manifestations reappear. It should only be considered, however, as an adjuvant measure—W. C. Wilson, G. D. Rowley, and N. A. Gray, *Lancet*, 1/1935, 1400.

**MUSCULAR DYSTROPHY**—Symptoms of progressive muscular dystrophy relieved in one case by cortin.—*J. Amer. med. Ass.*, 1/1934, 604.

**NEURASTHENIA**, with low temperature, low blood sugar and low blood pressure associated with deficiency of suprarenal cortex, treated by intravenous injection of cortex hormone—Otto Leyton, *Practitioner*, 1/1933, 466.

**PAGET'S DISEASE** is favourably influenced by treatment with adrenal cortex. The high blood phosphatase tends to fall to normal, with improvement in clinical symptoms—L. Berman, *Endocrinology*, 1936, 20, 226.

**VOMITING OF PREGNANCY**—Nausea and vomiting of early pregnancy treated by desiccated suprarenal cortex, orally, also temporary improvement from cortex extract; intravenously—Kemp, *Endocrinology*, 1932, 16, 434.

Improvement in 173 early cases of vomiting of pregnancy by subcutaneous injection of potent extract of suprarenal cortex for several days, followed by 9 to 12 gr. of desiccated suprarenal gland, reduced later to 6 gr daily—W. N. Kemp, *Med. Rec.*, N.Y., 1934, 110, 239.

Other references to adrenal cortex extract—F. C. Kendall, *J. Amer. med. Ass.*, 11/1935, 1487, A. Charpentier, *Lancet*, 11/1933, 921, "The Adrenals"—a review of the literature, *Prescriber*, 1935, 158.

The following are some proprietary suprarenal cortex preparations for use in the treatment of Addison's disease, etc.—

[P1] **Cortigen** (*Richter, London*) 1 ml represents 15 g suprarenal cortex substance. *Dose*—1 ml daily subcutaneously or intramuscularly.

[P1] **Cortin Organon** (*Organon Laboratories, London*) Liquid extract of suprarenal cortex (*Swingle and Pfiffner*) 1 ml equivalent to 50 g of whole gland.

[P1] **Eschatin** (*Parke, Davis, London*) 1 ml represents 40 g of suprarenal cortex. *Dose*—Severe cases, 10 ml intravenously every 3 or 4 days, in less severe cases, 1 to 5 ml subcutaneously.

[P1] **Eucortone** (*Allen & Hanburys, London*) 1 ml, is equivalent to 75 g of suprarenal cortex or approximately 110 g of whole gland.

[P1 87] **Guttæ Adaperlen** (*Endocrines Ltd., Watford*) Extract of suprarenal cortex, spleen, orchitic extract, and thyroid in a glycerinated solution. *Dose*—5 drops thrice daily. In asthenic conditions.

[P1] **Supracort** (*Paines & Byrne, London*) 1 ml represents 40 g of fresh suprarenal cortex. *Dose*—2 ml intravenously, increasing up to 20 ml daily.

**Kidney**.—Kidney substance has been given in nephritis and other kidney troubles, but the evidence of its value is conflicting.

Phenolphthalein should not be given simultaneously. Massive treatment said to be essential.

**Nephritin Tablets** (*Reed & Carnrick, Jersey City, Coates & Cooper, London*). Contains the hormones and internal secretions of the kidneys. *Dose*.—Four tablets four to eight times a day. *Dose* to be reduced as improvement occurs. For treatment of acute and chronic nephritis

## ÆTHER

*B P., P. Dan.*



*Syn* ÆTHER SULPHURICUS, ETHYL OXIDE (*U.S.P. XI*),  
SOLVENT ETHER

*Dose*.—15 to 60 minims (1 to 4 ml)

**Soluble** 1 in  $8\frac{1}{2}$  of water, and the ether similarly dissolves about the same amount of water. Is miscible in all proportions with alcohol. Ether is a solvent for a number of alkaloids, fats, resins, and of mercury perchloride and biniodide, also of bromine and iodine.

**Antidotes.** Treat as for poisoning by chloroform, see p. 365. For treatment of ether convulsions see below.

### Ether, Methylated.

Methylated ether may be prepared from duty-free alcohol and subsequently denatured by the addition of wood naphtha, or it may be prepared from industrial methylated spirit. It can be obtained with various specific gravities from 0.720 to 0.750. When prepared from methylated spirit it contains some methyl ether and may be used for spraying to produce local anæsthesia. It is *not* adapted for use as a general anæsthetic.

**Uses.**—Internally ether is a rapid stimulant in syncope. Is carminative and may relieve dyspepsia and asthma. Hypodermically it may save many cases of syncope, collapse, and shock from hæmorrhage and injury. It depresses nerve tissue, in very large doses it tends to depress muscle tissue, including cardiac muscle, but it never excites.

Ether has been used as an antiseptic dressing or irrigation for wounds, and it is used as a menstruum and vehicle for skin medication, on account of solvent action on sebaceous secretion. Ethereal tinctures and solutions of belladonna, capsicum, lobelia and menthol are prepared.

Care must be taken not to employ it near a light; its vapour is  $2\frac{1}{2}$  times heavier than air and very inflammable, and as an anæsthetic it has to be used freely.

For use as an anæsthetic, see below under Æther Anæstheticus.

**BRONCHITIS** (post-operative).—Intramuscular injection of 0.5 ml. of ether in 0.5 ml. olive oil, with the addition of a local anæsthetic, gave good results. One such injection daily recommended in every case of acute or chronic bronchitis without emphysema.—*Per J. Amer. med. Ass.*, 11/1925, 157.

**OTITIS MEDIA**, suppurative, treated by ether which is run into the affected ear and allowed to evaporate. In the cases not relieved chronic mastoiditis was revealed by X-rays.—*Med. J. Rec.*, Apr., 1926, 503, *per Prescriber*, 1927, 64.

**SCIATICA** has been treated by injection of ether with either cocaine or morphine subcutaneously into the sciatic nerve. 5 minim doses of ether with 2 minims of 1 in 12 cocaine, or morphine injection 3 minims, using a  $2\frac{1}{2}$ -inch needle.

**SHOCK.**—Recoveries from shock by intracardiac injection of ether 1 ml direct into the left ventricle successful in two cases. Response dramatic and gratifying—N Hay Bolton, *Brit med J* 11/1926, 482.

**WHOOPIING COUGH** treated by ether injected intramuscularly in the buttock Supposed to act by combating the spasmodic element of the disease 1 ml up to age of 7 or 8 months, and in older children 2 ml repeated daily or on alternate days—not invariably successful—*Lancet*, 1/1921, 1311 Most dramatically successful, also useful in broncho-pneumonia.—*Brit med. J. Epit*, 11/1922, 49

### **Mistura Ætheris cum Ammonia (B P C).**

**Dose.**— $\frac{1}{2}$  to 1 ounce (15 to 30 ml.).

Contains 30 m each of spirit of ether and aromatic spirit of ammonia in camphor water to 1 fl oz

*Syn* "PATENT", with 1 gr. of camphor per oz, "CAMPHORATED PATENT." A rapid stimulant *Gt. Örm H.* has (for child 1 year old) spirit of ether 3½ m, aromatic spirit of ammonia 3½ m, tincture of orange 2 m, chloroform water to 1 dr.

**Spiritus Etheris (B P)** Ether 33% *v/v*, in alcohol (90%)

*P. Belg IV* has ether 468, alcohol (94%) 532, *P Ital V* ether 1, alcohol (95%) 1, *FE VIII* ether 4, alcohol (90%) 1, *P Dan and P Helv. V*, ether 1, alcohol 30

**Dose.**—15 to 60 minims (1 to 4 ml)

The older formula is occasionally prescribed, viz —

**Spiritus Ætheris Compositus (B P. C)** *Syn* HOFFMANN'S ANODYNE, LIQUOR HOFMANNI, but the simple spirit of ether is now called Hoffmann's anodyne abroad

**Dose**—1 to 1½ drachms (4 to 6 ml) for a single administration, 20 to 40 minims (1.2 to 2.5 ml) for repeated administration.

An alcoholic solution of ether, about 1 in 8, with ethyl sulphate and ethyl hydrogen sulphate

### **Æther Anæstheticus (B P)**

*Syn.* ÆTHER PURIFICATUS, ÆTHER (*U S P XI*, *P Ned V*, *P Helv V*, *P Jap*, *P. Belg IV*, *P Ital V*, and *FE VIII*), ÆTHER PURISSIMUS, ÆTHER OFFICINARIUS, ÆTHER PRO NARCOSI

*Sp. gr.* 0.720. May now be made from duty-free rectified ethyl alcohol (*cf Lancet*, 1/1929, 295) Limit tests are included for peroxides, acetone and aldehyde, and methyl compounds, which may cause unpleasant post-operative effects

Æther Anæstheticus should be stored in amber bottles wrapped in black paper.

The "toxicity" which develops in ether, develops proportionately to the degree of oxidation by exposure to light and air, oxidised ether, in addition to producing local and necrosing effects, has distinct action on heart and central nervous system Toxic phenomena due to presence of peroxides The Anæsthetics Committee of the Roy Soc Med reported (Oct, 1926), "the purer the ether, the better the anæsthetic" Suggested that analyst's certificate of purity should accompany all anæsthetic ether—H E Laws, *Lancet*, 1/1927, 789, *Brit med. J*, 1/1927, 932.

Effects of acetaldehyde, peroxide, mercaptan and sulphide — *J Pharmacol*, 1926, 409

The rate of formation of peroxide increases greatly as the amount present increases—F H Carr, *Brit med J*, 11/1927, 664 See also *Lancet*, 11/1927, 1305

**Ether Convulsions**—A complication of ether anaesthesia; some fatal and non-fatal cases reported. Due to presence of impurities, acetaldehyde and "peroxide" in the ether. Impurities present on delivery and increased in amount by existing methods of ether administration. Question of ether purity requires further investigation. Exposure to light and air should be eliminated, and stale ether should be discarded. Use of amber glass in ether vapour bottles to protect from theatre lights, and metal tube projecting below level of ether replaced by bone or ivory. Convulsions treated by prompt ventilation of patient with oxygen containing 5% carbon dioxide—S R Wilson, *Lancet*, 1/1927, 1119. See also *Lancet*, 11/1927, 765.

Acetaldehyde and peroxide in ether *highly unlikely* to cause convulsions.  $\frac{1}{4}$ % said to be toxic (Wilson)—J Ross Mackenzie, *Brit med J*, 1/1931, 441.

The suggestion that ether convulsions are due to impurities in the ether has been found untenable in almost every instance in which the ether has been carefully tested, although when it was first put forward by the late S R Wilson there was much to support it. At present we must face the fact that ether convulsions, though still a rarity, are commoner than they were, and that their cause is unknown—*Lancet*, 1/1936, 157.

It is suggested that ether anaesthesia by upsetting the normal heat-regulating mechanism of the body may play a big part in the aetiology of ether convulsions by causing *heat stroke*. In three out of four cases which occurred at St Thomas's during 1935, the day temperature was excessively high, all the cases were preaxial and the post-operative temperatures were high, by stopping sweating an overdose of atropine tends to reduce heat loss, the hyperpnoea which  $\text{CO}_2$  produces removes not only ether but heat from the body, and its beneficial action in relieving convulsions may well be due to its action in accelerating heat loss. Convulsions are one of the manifestations of heat stroke. Pre-operative atropine should be limited to  $\frac{1}{16}$  gr. in children and young people with acute septic diseases and a temperature of over  $100^\circ\text{F}$ , especially in hot weather, and excessive coverings, especially mackintoshes, should be avoided for such patients in the theatre. To treat the convulsions,  $\text{CO}_2$  and oxygen should be given at once. If they do not cease within a minute Evipan Sodium should be given intravenously and cold sponges and ice applied to the body and face. If necessary the trachea should be intubated. Adrenaline and Coramine should be given to combat cardiac failure, and artificial respiration for respiratory failure.—R F Woolmer and S Taylor, *Lancet*, 1/1936, 1005.

## Anæsthesia with Ether

Ether is almost universally considered safer than chloroform, and the occasional sudden deaths in the early stages of induction with chloroform, from cardiovascular inhibition due to vagal stimulation or from ventricular fibrillation, are unknown with ether, as also is the delayed poisoning which may follow the administration of chloroform. On the other hand, ether is more irritant to the mucous membrane and induces hypersecretion of mucus in the air passages, consequently there is an increased liability to inhalation pneumonia. The secretion of mucus by the stomach and the activity of the salivary glands are also stimulated, thus increasing the tendency to post-operative nausea and vomiting. This excessive secretion is greatly diminished by the pre-operative injection of  $\frac{1}{16}$  gr. of atropine sulphate, but ether must not be used where there is any affection of the trachea, bronchi or lungs. It has a toxic action on the liver and kidneys, and prolonged administration is contraindicated if there is any lesion of these organs. Ether has less effect than chloroform on blood pressure, and capillary oozing is therefore less easily controlled. Induction by ether alone is very unpleasant, and some other anæsthetic such as nitrous oxide or admixtures of ether with chloroform in various

proportions are commonly employed until the second stage is reached.

For the production of anæsthesia ether may be administered by inhalation, in which the anæsthetic is vaporised by the patient's breathing, by insufflation, in which the previously vaporised anæsthetic is introduced directly into the mouth, pharynx or trachea by means of a suitable apparatus (*e.g.*, Shipway's), or rectally in oily solution. Other methods of administering ether have been proposed, such as delivery of ether vapour directly into the rectum, intravenous injection of a solution of ether in normal saline, or oral administration of 1 to 2 oz. of a mixture of equal parts of ether and liquid paraffin.

Administration as an inhalation anæsthetic may be by the "open," "semi-open" or "closed" method. In the former a piece of gauze tissue with a hole for the mouth and nose is placed loosely on the face, and above it is placed a wire mask (*e.g.*, the Schimmelbusch) covered with a layer of gauze and a further layer of gauze tissue with a hole through which the anæsthetic is dropped on to the gauze. Air can enter around the edges of the mask as well as through it, in distinction from the semi-open method in which the mask fits the face more closely and is covered so as to prevent access of air. In this method expired air is re-breathed, and there is less chilling from evaporation of the ether, an adequate concentration of anæsthetic is thus more easily obtained and induction occurs more rapidly. Air must be admitted periodically in order to prevent asphyxiation. In the closed method the patient breathes into and from a bag into which air and the vapour of the anæsthetic are admitted as required by the anæsthetist.

The smell of pure ether, if used for induction, may be masked by the addition of oil of orange. Gwathmey has recommended the use of 1 oz. of "essence of orange" (oil of bitter orange 1, dehydrated alcohol 3) and 3 oz. of ether in the hot-water bottle of the Gwathmey three-bottle apparatus.

When ether is to be employed for operations in which the presence of the mask would interfere, after induction by inhalation the anæsthetic may be administered by insufflation by means of a tube passed through the nose or mouth, according to the site of the operation, so that the vapour is delivered directly into the pharynx (intraparyngeal) or trachea (endotracheal). For endotracheal administration the insertion of the tube between the vocal cords is controlled with the aid of a laryngoscope, unless the condition of the mouth precludes its use. Intubation procedures may also be used with inhalation anæsthesia, but in this case the pharynx must be packed with lubricated plugs or in other ways, so as to prevent air being drawn in otherwise than through the tube.

Endotracheal anæsthesia is the method of choice for all operations on head, nose, mouth, and throat where satisfactory anæsthesia cannot be maintained with a free airway by the ordinary methods without inconvenience to the surgeon. When there is blood in the upper air passages it is a necessity.—S. Rowbotham, *Lancet*, ii/1926, 584.

### Rectal Ether Anaesthesia.

For rectal administration of ether the bowels are emptied by a cathartic given the previous evening and an enema on the morning of the operation. The anæsthetic is administered as a solution in olive oil, anæsthesia being complete in about 20 minutes and lasting for  $\frac{1}{2}$  to 1 hour. The following dosage has been recommended. For children under 6 years a 50% solution is used, allowing 1 oz. for every 20 lb. of body weight. This is non-irritating and no preliminary medication is wanted. Between 6 and 12 years use 55 to 65% solution without preliminary medication. Keep the patient quiet and allow 20 to 30 minutes for the full effect. Use 1 oz. for every 20 lb. body weight as before. Between 12 and 15 years use the same percentage and amounts, with possibly the addition of  $\frac{1}{2}$  gr. of morphine and  $\frac{1}{100}$  gr. atropine hypodermically as a preliminary. From 15 years upwards a 75% mixture is used with the same amount as before—1 oz. to every 20 lb. It will be seen, therefore, that for an adult weighing about 160 lb., 8 oz. of the mixture would be wanted (i.e., ether 6 oz. and olive oil 2 oz.). The 8 oz. should be passed in slowly, i.e., it should take 5 minutes. A maximum strength of 65% is now advised by Gwathmey—D. W. Buxton's "Anæsthetics." See also R. B. Coleman, *Brit. med. J.*, 1/1926, 943.

Rectal ether and olive oil has many advantages over inhalation, e.g., ease of administration, absence of apprehension in patient, and of coughing, retching, and straining, reduction of shock, and absence of post-operative vomiting—R. D. Laurie, *Brit. med. J.*, 1/1925, 1123.

Mixtures of equal volumes of ether and oil are the most suitable. Wash bowel immediately after operation and remove residual mixture. Smear Vaseline on buttocks and thighs to avoid irritation from escaping ether. Chief among the disadvantages is that depth of anæsthesia is not under such control as with inhalation; this may mean death to the patient. It causes irritation of the intestines, leading sometimes to severe and even fatal hæmorrhage. Must not be used in room with open flame. Evidence is not convincing that the use of 2 to 6 ml. of Gwathmey's 50% magnesium sulphate (i. postea) materially lessened the amount of ether required, but the action of morphine on the respiratory centre is synergistic with the ether and magnesium sulphate and numerous deaths have resulted from their combined use—R. A. Hatcher, *J. Amer. med. Ass.*, 1/1927, 2114, 2189, 2258.

In a series of 5000 anæsthesias slight diarrhoea occurred in only 6 cases and no deaths. (The retention enema now appears to consist of a 2 to 1 ether oil mixture with the addition of 2 dr. of paraldehyde.) A full description of technique is given. Has wider limits of safety than any inhalation method. Any pathologic condition of the bowel a contraindication—J. T. Gwathmey, *J. Amer. med. Ass.*, 1/1929, 447.

Safe and easily controlled, to use in all bad surgical risks. Leaves minimum of bad effects after operations lasting many hours—W. Wood, *Brit. med. J.*, 1/1929, 1156.

### Synergistic Method of Painless Childbirth (Rectal Ether Analgesia)—Gwathmey and others

This method depends on the supposed synergistic action of magnesium sulphate and ether, much smaller doses of both being necessary than when either is used alone. In obstetrics, when the os will admit three fingers, 0.006 g. ( $\frac{1}{16}$  gr.) of morphine in 2 ml. of a 50% solution of magnesium sulphate is injected intramuscularly. The injection is repeated in 2 or 3 hours if the pain is not relieved. At the same time, an enema composed of ether 70 parts, alcohol 8, quinine hydrobromide 0.6, and olive oil to 120 parts, is administered. Sometimes a mixture of ether 90 and chloroform 10 is used instead of ether alone. Forty-seven patients had painless labours; 13 were fairly free from pain; while 7 failures were due to giving the drug too early in labour. The failures emphasised the short duration of anæsthesia—4 to 5 hours. No



bad effects were noted on either mother or child.—Adler, "Anæsthesia in Obstetrics and Gynæcology," *Wien med Wschr*, May 8, 1926. *The method has now been modified (see below)*

Synergistic analgesia in childbirth is by no means safe in the hands of the unskilled. No method is suitable for universal use. The Gwathmey method mitigates the pains of labour, but no woman should be promised a painless labour. Should be used only in selected cases and by skilled anaesthetists.—R A Hatcher, *J Amer med Ass*, 11/1927, 2114, 2189, 2258

Great relief is given in 85% of cases and more or less relief in 10%. It is not claimed to give painless childbirth, but gives relief in the agonising part of the ordeal. No ill-results to mother or child. 5800 cases treated with satisfactory results.—J A Harrar, *Amer J Obstet Gynec*, April, 1927, 486-491.

The results of dog experiments show that Gwathmey's contention that synergism takes place between magnesium sulphate and morphine is erroneous. No satisfactory evidence has been brought forward to show that this synergism does occur in man.—H Beckman, *J. Amer med Ass*, 11/1925, 332

Gwathmey replies and produces extensive clinical evidence to prove that this synergism does occur in man—*ibid*, 1482

0.25 g per kilo the minimal effective dose causing depressant action. Addition of magnesium sulphate to colonic anaesthesia mixtures and its use in obstetric analgesia in the dosage now advised would therefore seem of no value.—I Newirth and G B Wallace, *J Pharmacol*, Feb, 1929, 170

#### Gwathmey's Modified Method.

The disadvantages are the intricacy of technique, the length of time that must be spent at the bedside, the necessity of isolating the patient, and the possibility of proctitis following the introduction of ether into the rectum.—J Beattie, *Lancet*, 11/1933, 37

On the one hand Gwathmey says quinine is an essential stimulant to the uterus in his system of analgesia. The quinine is given into the colon. But Bourne says it has no effect—on results of 2 cases. Balance in favour of Gwathmey's experience—20,000 cases.—A H Skinner, *Brit med J*, 11/1930, 621

Discussion of chloral hydrate *per os* and *per rectum*, opium, twilight sleep, and Adalin. Morphine  $\frac{1}{2}$  to  $\frac{1}{4}$  grain in 50% magnesium sulphate solution injected into the buttock has prolonged effect. The plain magnesium sulphate can be repeated without the morphine, and the sedative effect is prolonged. With such an ideal sedative, why try others? The effect of the morphine on the fetus is said to be fatal in some cases (Browne). Similar remarks apply to twilight sleep. Other anaesthetics chloroform, ether, nitrous oxide, ethylene, local and spinal, are reviewed.—A Louise McIlroy, *Brit med J*, 11/1930, 549

Benefit derived from Gwathmey's method in 97% of cases. Rectal ether 30% more efficient than "Twilight Sleep," and without danger to the infant.—O'Donel Browne, *Lancet*, 1/1931, 643.

The formula for the rectal mixture as now used is ether 2½ oz, quinine alkaloid 20 gr, alcohol 45 m, paraldehyde 2 dr, and liquid petrolatum or olive oil to 4 oz. The technique has been modified by the omission of the magnesium sulphate injection and the substitution of Nembutal by mouth, by the use of the degree of the patient's suffering instead of the amount of cervical dilatation as a time criterion for administration of sedatives and rectal instillations, by the substitution of a 5 to 10% solution of sodium bicarbonate (a heaped teaspoonful in a quart of water) for the soapsuds enema. If the Nembutal is not given within 8 hours after the initial enema the enema is repeated. The enema should not be given just before the rectal instillation—if this is unavoidable, any remaining water is siphoned back before the rectal instillation. Instead of the first two injections of magnesium sulphate the patient is given orally 3 gr. and 1½ gr. respectively of Nembutal,  $\frac{1}{4}$  or  $\frac{1}{2}$  gr. of morphine is usually given hypodermically with the second dose of Nembutal in a primipara in active labour, but if the labour is not uncomfortably active or is of the prolonged type, the second dose of Nembutal may be repeated once or oftener before the morphine is given (not more than 10 to 12 gr. in 24 hours). When the effects of the morphine begin to wear off the ether-oil-quinine solution is given *per rectum* and repeated as often as required, omitting the quinine after the second instillation. Omit morphine if delivery is anticipated within 4 hours—if it is anticipated within 4 hours the Nembutal and the rectal instillation are promptly

given simultaneously. During the administration of the instillation the patient is told to breathe deeply, with mouth open, and to draw up with the anal sphincter. After all the ether mixture is passed out of the catheter, the catheter is clamped to prevent air being drawn into the rectum. The catheter is then gently withdrawn and pressure made with a towel over the anus during 3 or 4 contractions. The instillation may be given at intervals of  $2\frac{1}{2}$  hours if necessary. At delivery, ethylene, nitrous oxide or ether is given by inhalation, but *not* chloroform. When the baby is born, if a gas-oxygen apparatus is used, all anæsthetic is cut off and 5% carbon dioxide and oxygen under pressure is given before the cord is cut. It is the safest of all satisfactory analgesias used to date. Several series of many thousands of cases have been reported, no maternal or infant mortality being attributed to its use. In addition, the patient rarely has more than a vague recollection of the labour. There are no major physical contraindications, it is not likely to prolong labour, and the baby suffers no ill-effects — J. T. Gwathmey and C. O. McCormick, *J. Amer. med. Ass.*, 11/1935, 2044.

## ÆTHYLIS CHLORIDUM

B.P., P. G. VI, U.S.P. XI.

$C_2H_5Cl$  - 64.56

*Syn.* CHLORYL ANÆSTHETIC, ÆTHANOLI CHLORIDUM (P. Belg. IV)

**Manufactured** by the action of hydrogen chloride on ethyl alcohol or industrial methylated spirit. If the latter is used it will contain a small amount of methyl chloride. The B.P. requires not less than 99.5% *w/w*  $C_2H_5Cl$ .

At ordinary temperatures this is gaseous, but condenses when slightly compressed into a colourless mobile liquid with a sweetish burning taste. Slightly soluble in water, readily in alcohol. Sp. gr. about 0.921 at 0.

**Antidotes.** Treat as for poisoning by chloroform, see p. 365.

**Uses.** Ethyl chloride has been successfully applied to ring-worm after washing with sodium bicarbonate and spirit of ether, applications must be repeated daily for a fortnight. It has also been used for warts, one application being sufficient for small ones. Its main use is as a local anæsthetic by freezing and as a general anæsthetic by inhalation. On account of its low boiling-point (about  $12.5^\circ$ ) and the intense cold produced by evaporation, it is effective as a local anæsthetic in minor surgery, also for neuralgia. The part should be washed with soap and then with alcohol or ether before applying. In dental cases the patient is instructed to breathe through the nose during operation, the part is well dried, and other parts protected. Its vapour is inflammable.

As a general anæsthetic ethyl chloride is not unpleasant, induction is rapid, occupying a minute or less, and recovery is also rapid although some patients experience nausea and *malaise* for a short time. As a single anæsthetic its main use is for minor surgery, such as tonsillectomy and dental extractions, in children, by whom nitrous oxide anæsthesia is badly tolerated owing to oxygen deprivation. In both adults and children it is useful for induction prior to maintenance with ether, the latter being administered as soon as breathing becomes regular. When used alone it produces

an anæsthesia lasting for 1 to 2 minutes followed by analgesia for a further 30 to 40 seconds. It may be administered by either the semi-open or closed method (*vide* Æther), the latter being adopted for children (*e g.*, using the Loosely bag).

Cardiac failure may occur as with chloroform, and there may be muscular spasm making artificial respiration difficult owing to rigidity of the chest wall

Open ethyl chloride a very convenient method of induction—portable, easy to patient, rapid in action, and safer than chloroform Useful for enucleation of tonsils, circumcision, and other minor operations, as also for major operations —J Ross Mackenzie, *Lancet*, 1/1927, 165

Nasal administration of ethyl chloride —R B. Gould, *Brit med J*, 1/1934, 1073.

DENTAL EXTRACTIONS under ethyl chloride at Gt Ormond St Hospital for Sick Children found satisfactory Closed method with a Loosely bag is used 60 to 180 seconds' surgical anæsthesia —H Sington, *Brit med J*, 1/1930, 217

**Ethyl Chloride with eau de Cologne** is available. The addition is thought to minimise post-narcosis effects

**Thillocologne** (*Thilo, Mainz, Coates & Cooper, London*) A brand of ethyl chloride and eau de Cologne

**Scented Ethyl Chloride** is not an improvement from an anæsthetic point of view on pure ethyl chloride It is just a "selling point" The essential virtue of an ethyl chloride is its purity When pure it is a stable compound of fixed chemical composition and cannot vary in quality —A Henning (Hedley & Co), *Brit med J*, 11/1933, 364

**Anestile** (*Bengué, London*) A mixture of ethyl chloride and methyl chloride for use as a local anæsthetic

**Somnoform** (*de Trey, Berlin, Amalgamated Dental Co, London*) is said to be a mixture of ethyl chloride 60%, methyl chloride 35%, and ethyl bromide 5% 60 g glass tubes with "valve stopper" for inhalation as an anæsthetic in dentistry Glass capsules contain 3 and 5 ml

If dangerous symptoms arise in administering proceed as directed under chloroform ethyl chloride

**Æthylis Bromidum** (*B.P.C., P.G. VI, Fr Cx, P Jap, P. Helv. V, P Belg. IV, F.E. VIII, P Ital V*) *Syn* HYDROBROMIC ETHER.  $C_2H_5Br = 109.0$

A colourless, very volatile liquid with a strong peculiar odour and a sweetish warm taste. Contains 1% of alcohol to prevent it becoming brown on exposure owing to decomposition and liberation of bromine. Sp. gr. 1.453 to 1.457 Bp about 38°

**Soluble** 1 in about 100 of water, and miscible with alcohol 90% and ether.

Has been used by inhalation for short general anæsthesia but is too potent a respiratory depressant.

For local anæsthesia it may be used as spray. For neuralgia it may be applied directly to the skin and covered for a short time. Capsules encased in cotton wool and silk, and containing 5 minims in each, are convenient for use by inhalation when crushed. They are useful in asthma and epileptic convulsions.

**Æthylis Dibromidum.**  $C_2H_4Br_2 = 187.9$  *Dose* —1 to 2 minims in alcoholic solution or oily solution hypodermically, or in gelatin capsules. A colourless liquid of sp gr about 2.18

**Æthylis Iodidum.**  $C_2H_5I = 156.0$ . *Syn.* HYDRIODIC ETHER *Dose.*—By inhalation, 3 to 5 minims (0.2 to 0.3 ml.).

May be obtained by distilling a mixture of alcohol, iodine and

phosphorus. A colourless, non-inflammable, heavy liquid (but liable to become coloured on exposure to air and light owing to liberation of iodine) with penetrating odour. B p.  $71^{\circ}$  to  $72^{\circ}$ ; sp. gr. about 1.943

**Soluble** 1 in 440 of water; miscible with alcohol and ether.

**Uses.** It is useful *inhaled* either alone or mixed with twice its volume of chloroform to relieve the dyspnoea of bronchitis, whooping cough and bronchial asthma. As it contains four-fifths of its weight of iodine, it forms a rapid means of saturating the system with this element, iodine can be detected in the urine 10 minutes after inhalation, and as long as 30 hours after: it neither impairs appetite nor weakens digestion.

In bronchial catarrh it induces sleep and promotes expectoration when inhaled. It is useful for inhalation in oedema of the glottis from catarrhal laryngitis. It acts as an antispasmodic in angina pectoris, spasmodic asthma and certain forms of nervous dyspnoea.

**Externally** 10 to 20% ointment with paraffin basis may be used (stronger may blister). The system may be saturated with iodine by painting the iodide on the calf of the leg or between the shoulders, and covering with impermeable dressing.

For inhalation it may be obtained in capsules enclosed in cotton wool and silk and containing 5 minims. The capsules are broken by pressure when required. Capsules are also obtainable containing 5 m. of ethyl iodide and 10 m. of chloroform.

**Capsula Ethylis Iodidi Composita (L.H.)** contains these ingredients with  $\frac{1}{2}$  gr. of menthol.

**MYCOTIC AFFECTIONS OF THE SKIN** treated by ethyl iodide inhalations. A large amount of iodine enters the blood stream and only a small amount is returned in the venous blood, hence the tissues are exposed to large amounts. Inhale 1 ml. in about 20 minutes. An apparatus is mentioned for controlling quantity. Fungus cured. Should be tried in asthma, hypertension, and tertiary syphilis.—*Brit. med. J. Epit.*, 1/1930, 62.

**Ethyl Iodide Sterules** (*Martindale, London*). Ampoules containing 5 m. and encased in cotton wool and silk, to be broken between the fingers and the vapour inhaled. Also available with chloroform 10 m. in addition, and with chloroform 10 m. and menthol 1 gr.

**Methyl Iodide.**  $\text{CH}_3\text{I}$  - 142.0

A colourless liquid (when first made) boiling at  $44^{\circ}$ . Sp. gr. 2.285. As a vesicant is even more powerful than cantharides.

Blisters may be produced in a few hours by rubbing in 15 to 20 drops.

**Æthylis Phthalas.** *Syn.* DIETHYL PHTHALATE.

$\text{C}_6\text{H}_4(\text{COOC}_2\text{H}_5)_2$ . A colourless, odourless, somewhat syrupy liquid with acrid taste. B p.  $290^{\circ}$  to  $300^{\circ}$ . Insoluble in water, soluble in alcohol 90% and in oils and aromatic hydrocarbons. Used as a denaturant in surgical spirits and perfumes.

**Methylis Chloridum.**  $\text{CH}_3\text{Cl}$  = 50.5. This gas, made by distillation of methyl alcohol, sodium chloride and sulphuric acid, is supplied compressed to a colourless liquid boiling at  $-21^{\circ}$ .

**Soluble** in water or alcohol, and readily soluble in ether and chloroform.

A local anæsthetic, valuable in neuralgia, sciatica and rheumatism. Spray the part for 5 or 6 seconds only. If effect too strong,

apply glycerin. Effect may be reduced by covering the part with a thin layer of cotton wool

**Antidotes.** Keep patient lying down and warm. Give fluids freely by mouth and enemas of 3% sodium bicarbonate with 5% dextrose. Avoid oils and fats. Oxygen inhalations if necessary. Potassium bromide, 60 gr doses, may be required for the convulsions.

**METHYL CHLORIDE POISONING.** Possibility of toxic effects in this country due to its increasing use in refrigerators. The symptoms of poisoning are progressive drowsiness and apathy with nausea, vomiting and abdominal pain. Possibly muscular tremors and toxic convulsions with marked cyanosis. Pupils usually dilated, ptosis and nystagmus have been noted, also amblyopia. Temperature rises, pulse and respiration rates are increased, blood pressure is lowered and the blood picture resembles primary anæmia. Anuria is usual in more severe cases and albuminuria occurs in about 50%, the urine is acid. Cerebrospinal fluid usually fairly normal but sometimes under pressure. *Treatment*—Fresh air, oxygen, alkalis, chloral or chloroform must not be used to control convulsions. Coramine as a cardio-respiratory stimulant. Rest in bed till temperature and pulse normal and nervous symptoms abated.—A. P. Gorham, *Brit. med. J.*, 1/1934, 529.

Intoxication occurring among workmen at refrigerating works employing commercial methyl chloride. A toxic agent, cumulative in action and detected in urine as ammonium formate.—H. M. Baker, *J. Amer. med. Ass.*, 1/1927, 1138. See also T. M. Legge and H. B. Porteous, *Brit. med. J.*, 1/1930, 414, 751.

**Methylene Chloride.**  $\text{CH}_2\text{Cl}_2$  - 84.9. Used as anæsthetic in Germany under the name of "Solæsthin." Unsuitable for complete narcosis, but may be used to relieve the pains of labour by a process of intermittent administration.—*Prescriber*, 1923, 319. See also *Brit. med. J. Erit.*, 1/1925, 18.

## AGAR

U.S.P. XI, P. G. VI, P. Svec. X, P. Helv. V, P. Dan., P. Jap. IV, F.E. VIII

Syn. AGAR-AGAR, JAPANESE ISINGLASS

*Dose.*—1 to 4 drachms (4 to 16 g.).

Consists of a dried decoction of various species of *Gelidium* (Rhodophyceæ). The sea-weeds are collected from rocks off the coast of Japan, bleached by exposure to the sun, boiled with water, and the filtered decoction concentrated by freezing or in other ways. The slabs so obtained are cut up and dried.

**Uses.** 1 in boiling water 200 forms on cooling a transparent jelly, suitable for invalids. It has little nutritive value—it is not digested—but is useful for treating constipation, especially of the type where the stools are hard and dry owing to complete absorption of liquid from the digestive tract. For this purpose it is best crushed into small pieces like bran—termed **Flaked Agar**. Clinical experience shows that finely-powdered or even sand-like powder is not efficacious. Teaspoonful doses occasionally of the dry substance in flake form sprinkled in a little moist food, e.g., stewed fruit, act as a mild aperient, softening the fæces, but should be employed at first in moderation, as it may possibly cause obstruction. By taking up moisture it increases the volume of the fæces and promotes peristalsis. It is used in preparation of

culture media for bacteria (*q.v.*), also for finishing calicos, silks, etc.

Vanilla, almond and raspberry flavoured flaked agar are prepared

**Thaolaxine** (*Sitsa, Paris, Wilcox, Jozeau, London*) Described as agar-agar with Rhamnaceous extracts, in form of scales, cachets, tablets and granules A laxative in treatment of chronic constipation

[P1] **Jubol** (*Chatelain, Paris, Spencer & Co, London*). Tablets of agar-agar with biliary and intestinal gland extracts, podophyllin, and extracts of aloes, hyoscyamus and belladonna Dose—3 tablets at bedtime

**Chondrus** (*B.P.C.*) Syn IRISH MOSS, CARRAGEEN (*P. Ned I., P. Belg IV, P. Helv V, P. Dan.*).

The dried sea-weed *Chondrus crispus* (Gigartinaceæ).

**Decoctum Chondri** (*B.P.C.*) Syn MUCILAGO CHONDRI Dose—1 to 4 ounces (30 to 120 ml) or more 1 in 40 A useful emulsifying agent, especially when an homogeniser is available Demulcent and nutritive, may be flavoured with sugar and lemon juice

**Cydonia** (*B.P.C., P. Helv V*) Syn QUINCE SELDS

The seeds of *Pyrus Cydonia* (Rosaceæ), containing about 20% of mucilage (cydonin) One part of the seeds with 40 of water yields a thick jelly used as mucilaginous agent in toilet preparations **Mucilage** of quince is official in some pharmacopœias, the strength varying from 1 in 25 to 1 in 100 The strength 1 in 25 of cold water or rose water is generally preferred It is prepared by macerating with the cold water for from  $\frac{1}{2}$  to 2 hours, and straining without expression **Decoction** of quince (1 in 80) is made by boiling for 10 minutes A preservative is necessary

**Fucus** (*B.P.C.*) Syn BLADDER OR SEA WRACK, KELPWARE The dried plant, *Fucus vesiculosus* (Fucaceæ) Contains the gelatinous substance, algin, and a variable proportion, up to 0.2%, of iodine It is recorded that a patient lost 20 lb in weight in 9 weeks when taking the liquid extract, without bad results.

In thyroid gland disease bladder-wrack was found to increase the thyroid secretion markedly

Chronic subcutaneous fibrosis has been treated by fucus combined with a more or less strict diabetic diet, exercise and massage

**Extractum Fuci** (*B.P.C.*), dose—3 to 10 grains (0.2 to 0.6 g), is a soft extract prepared with alcohol 45%

**Extractum Fuci Liquidum** (*B.P.C.*)

Dose.—1 to 2 drachms (4 to 8 ml) before meals 1 in 1

**Adiposettes** (*Riddell, London*) Ext fuc. vesic 5.9%, Ext frangul 8%, lecithin 1%, tetraboryl-bis-propan-triolester 30%, triphenylcarbinol-*o*-carbonic acid glycolate 10% Two to 5 tablets daily in obesity

## ALCOHOL ÆTHYLICUM

$C_2H_5OH = 46.05$ .

**Alcohol Dehydratum** (*B.P., U.S.P. XI, Fr. Cx., P.G. VI, P. Helv. V, P. Dan.*). Syn. ALCOHOL ABSOLUTUM.

Ethyl hydroxide, with not more than 1% *w/w* of water. Sp. gr. 0.7936 to 0.7967 representing not less than 99.4% *v/v* or 99% *w/w*.

*Fr. Cx.*—Sp. gr. must not exceed 0.79683 at 15°. *P Ned V* allows 2% of water; *U S P XI* sp. gr. 0.798.

**Antidotes** (ACUTE POISONING). Empty stomach by emetic or stomach tube. Keep patient warm, apply cold to head. Give 1 dr. of aromatic spirit of ammonia in 4 oz. of water, and a cupful of hot black coffee. Strychnine,  $\frac{1}{8}$  gr., hypodermically. Oxygen inhalations if necessary. Medicinal charcoal,  $\frac{1}{2}$  oz. in water, has been recommended.

REFERENCE. 10% carbon dioxide in oxygen administered with open slot mask, carbon dioxide increases respiratory excretion of alcohol, and oxygen will save life of rabbits given a dose of alcohol lethal to controls. Oxygen effective by speeding oxidation of alcohol rather than by relieving oxygen want. Clinically, results are encouraging, treatment recommended for acute alcoholism when danger of paralysis threatens life.—Robinson and Selesnick, *Lancet*, 1/1936, 50.

**Alcohol (95%) (B P)** *Syn* ALCOHOL (*U S P XI*, *P. Helv V*, *F.E. VIII*), ALCOOL ORDINAIRE or SPIRITUS RECTIFICATISSIMUS (*Fr. Cx.*), SPIRITUS RECTIFICATISSIMUS (*P Ital V*)

Contains 94.7 to 95.2% *v/v* or 92.0 to 92.7% *w/w* of ethyl hydroxide. Sp. gr. 0.815 to 0.817.

**Alcohol (90%) (B P)** *Syn* SPIRITUS RECTIFICATUS, SPIRITUS VINI (*P Austr*), SPIRITUS (*P Ned V*, *P. Helv V*)

Contains 89.6 to 90.5% *v/v* or about 85.7% *w/w* of ethyl hydroxide. Sp. gr. 0.832 to 0.835. Strength 57.80° O.P. (*i.e.*, 100 volumes contain approximately the same quantity of ethyl hydroxide as 157.8 volumes of proof spirit). It is generally manufactured commercially of higher alcoholic strength, *i.e.*, about 70 O.P., sp. gr. 0.809, containing nearly 95% *w/w* of ethyl hydroxide, and is diluted as required.

For various pharmaceutical purposes dilutions containing 70, 60, 45, 25 and 20% by volume are convenient.

*For Alcohol Dilution Tables see Vol II*

**Alcohol Dilutum** (*U S P XI*) Contains 41.5% *w/w* or 48.9% *v/v* of ethyl hydroxide.

*Note*—*U S P XI* orders on occasion a mixture of "Alcohol" 3 parts and water 1 part as menstruum in making tinctures and fluid-extracts. This is approximately equivalent to 70% by volume.

**Spiritus Tenuior**, PROOF SPIRIT (*B P*, '85), contained 57% *v/v* of ethyl hydroxide = 49% *w/w*; sp. gr. 0.920. It is legally defined as being such as shall, at 51°F., weigh exactly  $\frac{1}{4}$  of an equal volume of distilled water at 51°F. This corresponds to 49.28% *w/w* or, at 60°F., 57.10% *v/v*. Prepared by mixing 5 volumes of rectified spirit, sp. gr. 0.838, with 3 volumes of distilled water, the contraction being about 2.5%.

The greatest contraction occurs when quantities are in the proportion of 3 molecules of water and 1 of alcohol.

The addition of 100 to the number of degrees "overproof" gives the number of proof gallons, thus 100 gallons of 56 O.P. spirit = 156 proof gallons.

**Immature Spirits (Restriction) Act, 1915.**

1. (a) No British or foreign spirits shall be delivered for home consumption unless they have been warehoused for at least 3 years

Provided that—(b) This restriction shall not apply (i) to spirits delivered to a licensed rectifier, to a manufacturing chemist, or to a manufacturer of perfumes or to other persons licensed by Customs & Excise, (ii) to spirits delivered for scientific purposes

2. Nothing in this section of the Act shall interfere with the supply of Rectified Spirits of Wine for the purpose of making medicines to registered medical practitioners, to hospitals, and to persons and firms and bodies Corporate entitled to carry on the business of Chemist and Druggist

**DUTY AND REBATE TO CHEMISTS** A rebate of the difference between the present duty of 74/- per proof gallon and the old 1909 duty of 14/9 is allowed on immature spirit to duly qualified medical practitioners, duly registered pharmaceutical chemists and chemists and druggists on all duty-paid spirit used by them in preparations recognised as *medicines* by the Customs and Excise authorities. Rebate is also allowed on rectified spirits used for scientific research purposes approved by the Commissioners. The rebate is not allowed on tincture of orange, spirit of peppermint, mouthwashes and the like. A complete record of spirit used must be kept, and claims for rebate must be made to the local Customs and Excise authorities within 3 months of use. A minimum period to claim for is one month. The present increase of 59/3 per proof gallon over the old 1909 duty of 14/9 is equivalent to £4/13/7 per bulk gallon of S.V.R. 90%, 58 O.P.

**Duty Free Alcohol**, other than mineralised and industrial methylated spirit, is obtainable by permission of the Commissioners for use in any art or manufacture in which the spirit is required and where it is proved to their satisfaction that methylated spirit is unsuitable or detrimental, such as manufacture of esters, also for use by hospitals, schools, chemists, or other scientific workers for use in research or teaching. A bond must be given and the attendance of a Revenue officer to witness the denaturing of such supplies is requisite.—Commissioners of Customs and Excise

**Proof Spirit Conversion Factors** (I. C. J. Bird, *Chem & Drugg*, Dec. 27, 1919)

**METRIC MEASURE**

To express —

Litres of 90% Alcohol B.P.	in PROOF GALLONS	Multiply by	
70%	"	"	0.3471
60%	"	"	0.2697
45%	"	"	0.2312
20%	"	"	0.1733
	"	"	0.0767

**IMPERIAL MEASURE**

Gallons 90% Alcohol B.P.	in PROOF GALLONS	Multiply by	
70%	"	"	1.5779
60%	"	"	1.2263
45%	"	"	1.051
20%	"	"	0.7877
	"	"	0.3487

**QUANTITY OF SPIRITS WHICH MAY BE SOLD BY A CHEMIST WITHOUT LICENCE**

In view of the Immature Spirits (Restrictions) Act, 1915, the Commissioners of Customs and Excise reduced the quantity of duty-paid Spirits of Wine (including Absolute Alcohol), which may be sold without a licence, to 5 ounces fluid. Strict inquiries should be made by the pharmacist as to requirements.—*Pharm. J.*, 1/1922, 505

**EXPORT OF TINCTURES ON DRAWBACK (IMPERIAL AND FOREIGN).**

**Tinctures** (includes medicinal spirits, flavouring essences, perfumed spirits, toilet vinegars and waters, dentifrices, hair washes and brilliants) may be exported on drawback as merchandise, shipped or deposited in warehouse for use as ship's stores, and by Foreign and Imperial Parcels Post, direct from the premises of a person licensed to rectify or compound spirits (Licence, £15 15s per annum).

**Spirits of Wine** (includes "Absolute Alcohol," Ethyl Hydrate and Ethyl Hydroxide) may also be exported as above.



## QUANTITIES WHICH MAY BE REMOVED —

- (a) Not less than 2 bulk gallons of medicinal spirits and flavouring essences.  
 Not less than  $\frac{1}{2}$  bulk gallon of perfumed spirits (includes toilet water, hair washes, etc.)  
 Not less than 2 bulk gallons of Spirits of Wine
- (b) IF BY PARCEL POST — Each parcel not less than 0.125 bulk gallon, but not less than a total of 2 gallons packed for export in one day

Smaller quantities than the above may, on special application, be allowed by the local Surveyor, or by the Board, in special circumstances

SHIPPING BILLS to be filled up by exporter and presented to the local Customs and Excise Officer, who will examine and check all goods for export and seal the parcels or cases containing same.

**Uses.** Alcohol administered internally is a depressant to the central nervous system, the apparently stimulating effect being due to early inhibitory action on the higher centres such as those controlling self-criticism and judgment. It stimulates the secretion of gastric juice, thus increasing appetite when taken before meals and improving digestion when taken during meals. Continued excessive dosage leads to chronic gastritis. Strong alcohol causes increase in the rate and strength of the heart beat, and the skin vessels are dilated, causing a sensation of warmth. It should not be given to those in a cold atmosphere, since the vasodilatation and the depression of the heat-regulating centre cause a greater loss of heat. It is employed as a prompt reflex stimulant in fainting and collapse. In fevers, especially in acute pneumonia, it is valuable as a readily assimilated food, acting at the same time as a nerve sedative. Its food value is also useful in cases of diabetes when the diet must be restricted. Externally, alcohol is applied diluted in evaporating lotions in various superficial inflammations such as bruises, sprains, etc. Concentrated alcohol, e.g., surgical spirit, is applied for the prevention of bed sores, for hardening the nipples prior to lactation, and as an anhydrotic. It is extensively used for sterilising the skin and instruments, the maximum bactericidal effect is exhibited by a 70% dilution, stronger solutions are less effective because less able to penetrate the bacterial cell. An injection of 15 in. of alcohol 80 or 90% into the Gasserian ganglion is of value in trigeminal neuralgia, owing to destruction of nerve tissue, but the relief is rarely more than temporary. Similar injections have been tried in other neuralgias and in sciatica. As a gargle or spray diluted alcohol is a useful local application in tonsillitis, pharyngitis and diphtheria.

A compress of alcohol applied on cotton-wool so as to cover the whole abdomen and covered with a cold-water compress and a layer of impermeable tissue, the cold water being renewed hourly, has been used in the treatment of typhoid fever, especially of children.

**ANÆSTHESIA.** *General anaesthesia* by alcohol in glucose solution. Two solutions are used (a) Isotonic glucose solution, (b) 30 ml. of 96% ethyl alcohol in 70 ml. of 25% glucose solution. *Intravenous dose* is estimated according to patient's weight at 2 to 3 ml. of the 96% pure alcohol per kilo, but the maximum allowance is seldom exceeded. A few ml. of the (a) is allowed to run in first. —J. D. Constantin, *Lancet*, 1/1929, 1247, 1263, *ibid.*, 1/1930, 1393.

**CANCER.** The subarachnoid injection of a mixture of 60% absolute ethyl alcohol and 40% absolute methyl alcohol is of value for the relief of intractable

pain in advanced cancer. Puncture is performed in the interspace corresponding to the level of emergence from the cord of the nerves supplying the painful area, an amount of spinal fluid equivalent to the amount of alcohol to be injected being withdrawn. The head of the patient is kept at a lower level than the site of injection and the spine flexed to an acute angle as possible at this point. 0.8 to 2.0 ml of the alcohol mixture is injected slowly (at least 1 minute for each ml). The patient is then kept as nearly as possible in the same position for 4 hours, then flat in bed for 12 hours, and confined to bed for several days. No serious complication, but preoperative administration of phenobarbital 0.2 g and morphine 0.01 to 0.015 g is of value. Visceral pain is less amenable than somatic pain.—J. E. Dunphy, *New Engl J Med*, 1936, 214, 472.

**GANGRENE.** Periarterial injection of alcohol in gangrene of the extremities 2 to 3 m. at four points round circumference of artery and into outer coat.—S. Handlev, *Brit med J*, 11/1926, 1121.

**HÆMORRHOIDS.** Inject sphincter ani with local anæsthetic and inject each pile with  $\frac{1}{4}$  to 1 ml of 96% alcohol, starting with the higher internal piles. Piles completely shrivelled up by the next day.—*Per Practitioner*, 1/1929, 132.

**NEURALGIA.** Intractable trigeminal neuralgia or tic douloureux has been treated by alcohol injections (80% usually employed) around the supraorbital notch. Give hyoscine  $\frac{1}{4}$  gr and morphine  $\frac{1}{4}$  gr 20 minutes in advance. Prior to the alcohol a few drops of 3½% eucaine to assist in locating the nerve trunks.

1100 cases treated over 23 years. Injection of the nerve at the foramen ovale, or rotundum, relieves pain for at least a year, with injection of ganglion if alcohol returns within 18 months.—Wilfred Harris, *Lancet*, 1/1913, 881, *ibid*, 11/1922, 122, *ibid*, 1/1931, 569.

Danger of injections for neuralgia. Novocain preferable to general anæsthetic.—*Lancet*, 11/1923, 1407.

Pain will not return in the majority of cases if anæsthesia in the central distribution of the fifth nerve persists for a month. Definitely indicated for patients who have had radium treatment for cancer of the face, the absolute indication being carcinoma of the maxilla or of the tongue. The treatment usually gives permanent relief, if enough alcohol is injected.—G. M. Dorrance, *J Amer. med Ass*, 11/1924, 1678.

Trigeminal neuralgia. Hartel injection route, using alcohol, into the region of the Gasserian ganglion.—L. Morris, *Lancet*, 1/1931, 122.

Wilfred Harris now uses 2% Novocain to test cutaneous anæsthesia. Important to inject not more than 2 minims of alcohol at a time and test anæsthesia with a pin before injecting more. To correct commencing anæsthesia of the eye (causes "blinking") push needle another  $\frac{1}{4}$  inch into ganglion, but before injecting watch for cerebrospinal fluid—if this appears withdraw partly and reinsert in a more backward direction.—*Brit. med J*, 11/1932, 88.

**PROLAPSE OF RECTUM** treated by injecting 1.5 ml. of absolute alcohol on each side or into the perirectal tissue at a depth of 2 to 2½ inches.—I. Findlay and J. B. Douglas Galbraith, *Lancet*, 1/1923, 76.

Injection treatment using absolute alcohol, 1.5 ml being injected on each side into the perirectal tissues at a depth of 2 to 2½ inches, the needle being inserted about a  $\frac{1}{4}$  inch from the anal margin. A pad is then placed in the perineum and kept in position by strapping the buttocks, the pad and strapping being reapplied daily for a week.—I. Findlay, *Brit med J*, 11/1934, 330, H. Williamson, *ibid.*, 331.

[P2] **Alcohol Ammoniatum (B.P.C.).** A 10% v/v solution of ammonia gas in alcohol. Is used in the preparation of parogens.

**Lotio Evaporans (B.P.C.).** Alcohol, 1 in 8, with ammonium chloride and distilled water.

**Spiritus Frumenti.** Whisky prepared by distillation of fermented grain—barley, wheat, rye, Indian corn. Sp. gr. is usually about 0.925. It usually contains about 40% v/v of alcohol, 0.1 to 0.2% of higher alcohols, 0.03 to 0.08% of esters, 0.2 to 0.8% of volatile acid with traces of furfuraldehyde and other substances.

**U.S.P. XI.**—From wholly or partly malted cereal grains and not less than four years old, 47—53% by vol.

**Whisky Defined.**

According to the findings of the Royal Commission on Whisky (1909), "Whisky is a spirit obtained from distillation from a mash of cereal grain

saccharified by the Diastase of Malt." This decision allowed the name Whisky to be applied to the patent-still spirit in addition to the old pot-still spirit. The strongest objection to patent-still spirit was its "tameness" and lack of response to ageing, as a result of which many foreigners regard whisky as plain alcohol, and are astonished at the superior taste and aroma of matured whisky — "Veteran," *Harper's Wine and Spirit Gazette*, Oct 31, 1931

Malt whisky is made entirely from barley, a fine hard grain being selected. In patent distillation, Indian corn or maize, rye and barley are all employed. A pure malt whisky is a mixture of heavy highland malts of 10 to 14 years' maturing and of lighter malts of from 6 to 10 years' maturing. Spirits do not improve in bottle.

**Spiritus Vini Gallici.** BRANDY. Contains 40 to 50% (or 60% in case of good Cognac) by volume of alcohol. *P. Helv. V.* requires a minimum of 50%.

Contains about 0.05 to 0.15% of higher alcohols, 0.1 to 0.15% of esters, 0.05 to 0.2% of volatile acid with traces of furfural and other substances.

**Spiritus Vini Vitis** (*U.S.P. XI*) has 48 to 54% by vol., and is not less than 4 years old.

### **Mistura Spiritus Vini Gallicus (B.P.C.)**

*Dose.*—1 to 2 ounces (30 to 60 ml.), as a draught.

2 oz. contains about  $\frac{3}{4}$  oz. of brandy with yoke of egg, sugar and cinnamon water.

### **Vinum Xericum (B.P.C.)** *Syn.* SHERRY-TYPE WINE.

Prepared by the fermentation of grape juice. It may be either true sherry, prepared only in Spain, or wine of a similar type prepared elsewhere, such as in Australia or South Africa. It contains not less than 16% *v/v* of alcohol.

**Vinum Xericum Detannatum (B.P.C.)** is sherry-type wine detannated with gelatin. It does not yield precipitates with alkaloidal solutions.

### **Alcohol Allylicum.** $\text{CH}_2 = \text{CH} \cdot \text{CH}_2 \cdot \text{OH} = 58.05$

A colourless liquid miscible with water, with a pungent odour and burning taste. It inhibits bacterial growth.

Open chain derivatives containing unsaturated carbon atoms are more toxic than isomeric saturated bodies. Thus allyl alcohol is 50 times more toxic than normal propyl alcohol.—O. C. M. Davis, *Brit. med. J.*, 11/1922, 12.

## **ALCOHOL AMYLICUM**

*B.P.C.*

$\text{C}_5\text{H}_{11} \cdot \text{OH} = 88.09$

Obtained by purifying fusel oil, and consists of a mixture of about 90% of primary isoamyl alcohol,  $(\text{CH}_3)_2\text{CH} \cdot \text{CH}_2 \cdot \text{CH}_2 \cdot \text{OH}$ , and 10% of primary active amyl alcohol,  $\text{CH}_3 \cdot \text{CH}_2 \cdot \text{CH}(\text{CH}_3) \cdot \text{CH}_2 \cdot \text{OH}$ . Occurs as a colourless liquid with characteristic odour. B.p.  $128^\circ$  to  $132^\circ$ . Sp. gr. 0.815 to 0.817.

**Soluble** slightly in water; miscible with fixed and volatile oils and with alcohol, ether, chloroform and other organic liquids.

**Amylis Acetas (B.P.C.)**  $\text{CH}_3 \cdot \text{COOC}_5\text{H}_{11}$ . A colourless, inflammable liquid with a powerful, pear-like odour. Very slightly **soluble** in water, miscible with ether, alcohol 90% and other organic liquids.

[P1] **Amylis Nitris** (B.P., U.S.P. XI, P. Ned V, P. Austr., P. Belg. IV, P. Jap., P. Hung., P. Ital. V, P.G. VI, P. Svec. X, F.E. VIII, P. Helv. V, P. Dan.). Syn. AMYLIUM NITROSUM, AZOTITE D'AMYLE.  $C_5H_{11}NO_2 = 117.15$ .

**Dose**—By inhalation, the vapour of 2 to 5 minims (0.12 to 0.3 ml.); up to 10 minims may be inhaled. Very rarely it has been given by the mouth in doses of  $\frac{1}{2}$  to 1 minim (0.03 to 0.06 ml.), or hypodermically in doses of 1 to 5 minims (0.06 to 0.3 ml.)

A yellowish ethereal liquid with a peculiar, not disagreeable odour; produced by the action of nitrous acid on amylic alcohol boiling between  $128^\circ$  and  $132^\circ$ , and consists chiefly of the nitrites of isobutylcarbinol,  $(CH_3)_2CH \cdot CH_2 \cdot CH_2OH$ , and *sec*-butylcarbinol  $(C_2H_5)(CH_3)CH \cdot CH_2OH$ . Should be kept cool; on exposure to the air it becomes comparatively inert

**Insoluble** in water, miscible with alcohol and ether.

Thin glass capsules, encased in cotton-wool and silk, are made containing usually 3 minims, also 1, 2, 4, 5, 6 or 10 minims

In use the capsule is broken, the liquid soaks the cotton-wool, and the vapour can be inhaled

**Incompatible** with alkaline carbonates, potassium iodide, bromides and ferrous salts

**Antidotes.** Empty stomach by emetic (if amyl nitrite has been swallowed) Keep patient lying down and warm Apply artificial respiration if necessary and give inhalations of oxygen, alone or with 5% carbon dioxide Injections of adrenaline or ephedrine

**Pharmacology.** Amyl nitrite dilates the vessels and lowers blood-pressure The vessels of the head and neck are most affected, and within 30 to 40 seconds after inhalation or swallowing a dose, the face flushes, the heart beats become rapid and violent, and the head and neck perspire

The effect on the pulse can be shown within 10 seconds of inhalation, but lasts usually for 2 to 3 minutes only. The rapidity of action is due to the large area of the lungs absorbing the drug—roughly 100 sq metres—and to the thinness of the membranes (about  $\frac{1}{1000}$  mm) separating the air of the pulmonary vesicles from the blood.

The action of amyl nitrite and the nitrites generally in relaxing arterial tension was discovered experimentally by Rutherford and Gamgee. This led Sir Lauder Brunton to the discovery of its value and that of nitroglycerin for relief of anginal spasm.

**Uses.** It is mainly used for the relief of attacks of angina pectoris, acting by dilatation of the coronary artery. Its use is contraindicated in coronary thrombosis Asthma is sometimes relieved by inhalation owing to the action of amyl nitrite in relaxing the peripheral vasoconstriction which is an essential factor in the bronchial vascular distension responsible for the respiratory obstruction In asthma, however, as also in arteriosclerosis, other nitrites are preferred owing to their more prolonged action. In chloroform syncope amyl nitrite affords the quickest means of

restoring the heart's action. It may be used in status epilepticus, and will frequently abort an epileptic fit if inhaled during the aura of an attack. Hæmoptysis can in most cases be immediately arrested if amyl nitrite is inhaled as soon as the first signs of blood are seen in the sputum. Any subsequent excitement can be controlled by morphine  $\frac{1}{4}$  gr hypodermically. It is also valuable in cerebral and in post-partum hæmorrhage, and may be used to control menstrual flooding, *e.g.*, in tiding over fibroid disease until the menopause. It may also be used in migraine and neuralgic dysmenorrhœa and in the spasms of tetanus, false croup, whooping cough and strychnine poisoning. Inhalation of 1 minim may be used in infantile convulsions and may cut short the attack. It is a powerful agent for causing relaxation of uterine spasms and hour-glass contraction, whether natural or caused by ergot. Externally amyl nitrite 10% in alcohol 90% has been applied to the scalp on alternate nights to assist the action of stimulant hair lotions such as pilocarpine hair lotion. Local application supplemented by inhalation has been used successfully in the treatment of urticaria, eczema and other skin diseases.

**ANGINA PECTORIS** Angina is a symptom relieved by certain drugs which dilate the coronary arteries and improve blood supply to the heart. On this supposed effect of amyl nitrite, etc., is based the more widely accepted view of the pathology of the condition that it is caused by disease of the coronary vessels. The condition is, however, a symptom-complex and that ill-defined—Harlow Brooks, *Brit med J*, i/1931, 18.

Observations upon angina pectoris. Nature and distribution of the pain, duration of attack, ætiology—the current theory (Allan Burns) is that it results from muscular anoxæmia—diagnosis, prognosis, treatment. If the blood pressure is raised during attacks the nitrites are useful, but useless if it is not raised. Sedatives—morphine—John Cowan, *Brit med J*, i/1931, 879.

No reason why amyl nitrite and nitroglycerin should not be used indefinitely. They enable patient to lead a more normal life—Maurice Campbell, *Practitioner*, i/1931, 35.

**AORTIC INCOMPETENCE** of syphilitic origin. A man while lying quietly in bed suddenly developed acute pain, described as "knife-like and stabbing," in right shoulder, spreading over the precordium and down left side. "During the attack he had an expression of intense agony on his face. The whole affair was relieved in about 2 minutes by amyl nitrite." About 20 minutes later the pain returned, but amyl nitrite again afforded relief with no return of pain. 12 days later there was another attack, accompanied by dyspnoea and a pulse-rate of 124; amyl nitrite again gave almost instant relief—C. F. Coombs, *Brit. med J*, i/1928, 1012.

**POST-PARTUM HÆMORRHAGE** Invaluable, but must be used with caution. During parturition chloroform, as is well known, is safe owing to the tension within the abdominal cavity, but it is dangerous given shortly after delivery on account of the sudden withdrawal of this tension, which is liable to cause paralysis of the vasomotor mechanism, thus permitting the blood to accumulate in the splanchnic area. L. Hill has pointed out that amyl nitrite, if incautiously given, may produce the same effect.—A. T. Brand and J. R. Keith, "Clinical Memoranda for General Practitioners," 1923.

**SKIN AFFECTIONS.** Eczema and other skin affections improved remarkably by inhalation, the arterial hyperæmia being the curative factor. Local treatment is also promising and brilliant results are stated to be obtained in urticaria and in senile pruritus.—*J. Amer. med. Ass.*, i/1925, 1241.

**UTERINE SPASM** In cases of "contraction ring" amyl nitrite inhalation is the one method of treatment which alone seems to meet with universal success. Description of 5 cases, inhalation followed by delivery.—C. R. Croft, *Lancet*, ii/1928, 167.

[P1] **Amyl Nitrite Sterules** (*Martindale, London*) are capsules of amyl nitrite for inhalation, and are available containing 1, 2, 3, 4, 5, 6 or 10 minims, the 3-minim size being satisfactory in most cases.

**Amyleni Hydras** (*B.P.C., P. Helv. V, P. Ned. V, P.G. VI*)  
*Syn.* DIMETHYL-ETHYL CARBINOL, TERTIARY AMYL ALCOHOL  
 $(\text{CH}_3)_2\text{C}_2\text{H}_5\text{C}\cdot\text{OH} = 88\cdot09$ .

*Dose.*— $\frac{1}{2}$  to 1 drachm, flavoured with liquorice. The Continental pharmacopœias have maximum single dose 1 dr approx, maximum in 24 hours 2 dr. May be given in capsules or in a mixture.

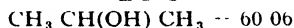
A colourless liquid, of pungent taste and odour, resembling a mixture of paraldehyde and camphor.

**Soluble** in 8 of water, miscible with alcohol 90%, ether, chloroform and glycerin.

**Uses.** Hypnotic, occupying a position between chloral and paraldehyde; a stage of excitement may precede hypnosis. Capsules contain 10 minims in each. It is used as a solvent for the concentrated solution of Avertin. (*See page 299*)

## ALCOHOL ISOPROPYLICUM

### B P C



*Syn and Prop Name* SECONDARY PROPYL ALCOHOL, DIMETHYL CARBINOL, AVANTINE (*Howards & Sons, Ilford*)

### Isopropyl Alcohol Regulations, 1927

*Manufacturers, sellers and users of Isopropyl Alcohol in Great Britain and Northern Ireland must render returns to the Customs and Excise authorities, showing the quantity manufactured, used, and/or sold, together with the names of purchasers, and the purposes for which the Alcohol has been used*

A colourless liquid with spirituous odour and somewhat burning taste, containing about 96% *v/v* (94% *w/w*) of  $\text{C}_3\text{H}_8\text{O}$ . Sp. gr. 0·808 to 0·810, b p 80·5° to 82·2° (*B P C.* gives sp. gr. 0·810 to 0·812, b p 80·5° to 81·5°). It is also obtainable containing 98 to 99% *w/w*, with sp. gr. 0·793 to 0·795 and b p. 81·5° to 82·4°. In the anhydrous condition it has sp. gr. 0·788 and b p. 82·4°. It is miscible with water or ethyl alcohol in all proportions.

**Preparation.** It may be made synthetically, *e.g.*, by reducing acetone, using sodium amalgam or by passing acetone and hydrogen over a metallic catalyst. It is also obtained from propylene, a by-product of the petroleum industry in the U.S.A., by absorbing the olefine gases, containing propylene, in sulphuric acid and hydrolysing the resulting alkylsulphuric acids.

The rectified product contains 91% of the alcohol, with dry caustic soda it can be made anhydrous.

**Pharmacology.** Isopropyl alcohol is twice as toxic as ethyl alcohol intravenously in cats. Vapour of isopropyl alcohol did not kill rats exposed to fumes (*cf.* methyl alcohol). 50 ml given *per os* to a dog weighing 6·5 kilo caused serious incoordination, but the animal completely recovered. Applied to wounds in concentration up to 50% allowed same to heal normally. —*Pharm. J.*, 11/1922, 272

It is stated to be less toxic than *n*-propyl alcohol. Administration by mouth produces narcosis, in larger doses anæsthesia, finally coma and death. Very little is absorbed by inhalation or through the skin.—*J. chem. Soc. Abstr.*, 1922, 1093.

**Uses.** It is safe internally in small doses in dilute form, and could be used for making tinctures of drugs. It has been suggested as a surgical antiseptic and could, no doubt, replace ethyl alcohol in many surgical and medical procedures. In commerce, it is also suitable as a solvent for crystallising and for extract manufacture. It is now largely used in perfumery and in the culinary arts (flavouring essences). *Externally*, it has been found harmless to the skin and hair, and within reason it can be inhaled mixed with air.

*The above remarks apply, it should be noted, to isopropyl alcohol. The isomeric NORMAL, OR PRIMARY, PROPYL ALCOHOL,  $\text{CH}_3\text{CH}_2\text{CH}_2\text{OH}$ , is more toxic and unsuitable for making tinctures and the like*

(For particulars with reference to the preparation and composition of various isopropyl tinctures and spirits made by W. H. Martindale, see Edition XX, p. 120.)

## ALCOHOL METHYLICUM

*B.P.C.*

$\text{CH}_3\cdot\text{OH} = 32\cdot03$ .

*Syn. METHANOL.*

*Dose* —30 to 60 minims (2 to 4 ml.)

Methyl alcohol is synthesised on a commercial scale from water gas (a mixture of carbon monoxide and hydrogen) under pressure at about  $400^\circ$  in presence of a catalyst, usually metallic copper containing 10% of zinc oxide.

Synthetic methyl alcohol has been used as an anti-freeze mixture for radiators. Toxic effects in U.S.A. —*Brit. med. J.*, 11/1930, 745.

If absolute and "acetone-free," methyl alcohol has sp. gr. 0.796, but it is not allowed by the Excise to be retailed pure unless duty-paid. *B.P.C.* requires the sp. gr. to be not higher than 0.799. The commercial substance known as WOOD NAPHTHA, PYROXYLIC SPIRIT, or WOOD SPIRIT, is 60 to 90% pure, and contains acetone and other empyreumatic impurities. The variety used for denaturing alcohol contains 72% *v/v* of methyl alcohol. It is a solvent of pyroxilin. The methylated spirit licence is not necessary for the sale of wood spirit, but that licence does not, of course, cover the sale of pure methyl alcohol.

**Antidotes.** Empty stomach by emetic or by stomach tube, using 5% sodium bicarbonate solution. Give water freely. Keep patient warm. Strychnine,  $\frac{1}{2}$  gr., hypodermically.

### **Spiritus Methylatus, Mineralised or Denatured.**

Since May, 1924, this consists of a mixture of spirit 90%, wood naphtha (methyl alcohol) 9.5% and crude pyridine 0.5%, with in addition  $\frac{3}{4}$ % (0.375%) of mineral naphtha ("petroleum") and a small proportion of methyl violet to colour. It forms an opaque mixture with water.

**Caution.** It is not well adapted for local use—*e g.*, for bed sores.

It caused dermatitis amongst surgeons of Manchester Royal Infirmary, and amongst barbers of that city. Pyridine was probably the cause of the trouble (The pyridine was added to render the spirit undrinkable.)

Denaturalised spirit in Germany contains  $2\frac{1}{2}\%$  of a mixture of wood spirit 80 parts, pyridine bases 20 parts (This amounts to 0.5% of pyridine as in British (1924) methylated spirit.)

**Spiritus Methylatus Industrialis (B P).** Industrial methylated spirit was introduced by the provision of the Revenue Act, 1906. It is simply a mixture of plain "spirits" with one-nineteenth of its bulk (5% *v/v*) of wood naphtha (methyl alcohol), and is of the quality known as 66 O P industrial methylated spirits. It is considerably purer than the mineralised spirit and of greater utility for manufacturing purposes.

**Spiritus Methylatus Industrialis sine Acetono (B P C)**  
INDUSTRIAL METHYLATED SPIRIT (ACETONE-FREE)

Is of the same strength as industrial methylated spirit, but the denaturant used is practically free from acetone. It is compatible with iodine, with which industrial methylated spirit containing acetone yields irritating vapours.

**Spiritus Chirurgicis (B P C).** SURGICAL SPIRIT.

Formula No. 1 contains industrial methylated spirit with castor oil, methyl salicylate and ethyl phthalate. Formula No. 2 contains industrial methylated spirit with castor oil, mineral naphtha and ethyl phthalate.

These are the only formulæ which are at present approved by the Board of Customs and Excise, and there are no restrictions on purchase or sale by chemists. Surgical spirit made to any other formula, such as that of the *N I F*, may be supplied on prescription only; it cannot be purchased from the wholesaler but must be made by the chemist as required, and is subject to the statutory regulations relating to dispensing prescriptions for preparations containing I M S.

**Sp. Antisepticus (N I F).** SURGICAL SPIRIT

Castor oil 96 m, boric acid  $38\frac{1}{2}$  gr., industrial methylated spirit to 8 oz.

Where the term "Surgical Spirit" is used in a *N I F* prescription without qualification, it should be interpreted to mean Sp. Antisepticus (Surgical Spirit), *N I F.*, 1933. Where the term Surgical Spirit No. 1 or Surgical Spirit No. 2 is used, it should be interpreted to mean formula No. 1 or No. 2 included under *Spiritus Chirurgicis, B P C.*, 1934.—Ministry of Health Circular Letter, I C L. 844, per *Pharm J.*, 1/1935, 101.

Surgical spirit may not be used as a base in the manufacture of other preparations. It must be sold exactly as received from a wholesaler—*Pharm J.*, 1/1926, 323, 536.

**Methylated Spirit Drinking.** Wood alcohol poisoning is generally accompanied by blindness. The end product excreted by the kidneys is formic acid. This reduces Fehling's solution, so its presence may interfere with diagnosis.—S. L. Ziegler, *Lancet*, 11/1921, 618.

It is said that blindness may follow even 7 or 8 g., but the toxic dose is less. Numerous references to the subject in *Edn XVII*, p. 121.



In 1926 2000 people died in U.S.A. as a result of drinking so-called whisky prepared from denatured alcohol—*Lancet*, 1/1927, 89

Memorandum dealing with resolutions under consideration by the Convention of Royal Burghs, anent the prevalent evil of methylated spirit intoxication. Complicated regulations proposed by the Convention, under police control—*Pharm. J.*, 1/1922, 387.

Toxic effects of methylated spirit—Sir William Willcox, *Lancet*, 11/1929, 124

RED BIDDY No evidence of manufacture or sale in Scotland of admixtures of red wine and methylated spirits, though reason to believe such mixtures are made by purchasers of cheap red wine. Considerable quantity of latter made in Leith—*Pharm. J.*, 1/1930, 218

RED LIZZIE Known as Lisbon Wine in South and East London. Caused acute cirrhosis of the liver—Sir William Willcox, *Brit. med. J.*, 1/1931, 596

"Red Liz" made with the current S.V.M. and Lisbon Wine—*Pharm. J.*, 11/1930, 306

The regulations governing the use of both methylated and industrial spirit have been revised and consolidated by the following—

**METHYLATED SPIRITS REGULATIONS, 1930.** *In operation since January 1, 1931 S.R. and O., 1930 No. 832 (Abstract of salient points)*

NOTICE No. 50 (BUFF COLOUR)—Applicable to all users

34. Methylated Spirits may not be purified

39. Methylated Spirits may not be recovered or re-distilled, except by sanction. Must be kept under lock, or to satisfaction of Officer. Bottles to be labelled "For external use only," or "Not to be taken," or otherwise to the same effect

NOTICE No. 53 (BUFF COLOUR) Sale of Industrial Methylated Spirits for medical and scientific purposes by wholesale chemists and dispensing chemists under Regn. 50

(1) Any wholesale or dispensing chemist with a Methylated Spirits Retailer's Licence may, on application, receive Industrial Methylated Spirits in quantities not exceeding 4 gallons for sale to authorised users on receipt of requisition in the official form. This applies to all sales of Industrial M.S. to dispensing chemists, and the limit of 1 gallon is now withdrawn

May be sold in quantities not exceeding  $\frac{1}{2}$  gallon at a time to a medical practitioner, dentist, veterinary surgeon, hospital or nursing home, on a signed order—purchaser need not hold official authority or submit a requisition, but order must be signed by a doctor, chemist, or veterinary surgeon. This does not cover supplies to dispensing chemists

(2) Industrial M.S. may be exported in quantities not exceeding 4 gallons. Requisitions unnecessary, and the spirits may be supplied merely on customer's order

(3) Every wholesale or dispensing chemist wishing to sell Industrial M.S. must apply for special authority, whatever authority he may already hold

(4) Regn. 50 requires Industrial M.S. for sale in accordance with para. (1) and (2) to be kept apart from I.M.S. used for other purposes, a separate stock being kept under proper control, and an account kept of this separate stock. Accounts must be balanced monthly, orders and documents must be kept for two years and the contents of bottles or other containers must be labelled "Industrial Methylated Spirits"

NOTICE No. 54 (GREEN COLOUR)—Applicable to dispensing chemists

1. Where already authorised to receive Industrial M.S. for dispensing, he is automatically and without further application entitled to use and dispense I.M.S. as at (i) and (ii) para. 2, while being liable to conditions in para. 3 and 4. If existing authority covers use of I.M.S. in making articles not in Second Schedule he will continue to be entitled to use I.M.S., but as from Jan. 1, 1931 no authority held prior to that date to sell I.M.S. to other chemists is valid, and special authority must be obtained

2. All future applications must be made on special form (Ex. No. 225A), and grant of authority will convey (i) right to make and sell articles in Second Schedule, (ii) right to make and dispense on prescription only articles not scheduled or authorised, or I.M.S. subject to Regulations and Conditions in para. 4. Application may also include request for authority to use I.M.S. in making other articles or for other specified purposes

3. **Permits** received from methylators must be kept and delivered to Officer M.S. must not be purified, except with special sanction. M.S. must be kept under proper control. All containers to be labelled "For external use only," or "Not to be taken," or otherwise to the same effect. Return to be made once a year.

4. Articles not in the Second Schedule or authorised may be supplied only on the following conditions —

- (i) Dispensed only on signed order or prescription by medical practitioner, dentist, or veterinary surgeon
- (ii) A prescription or order for I M S diluted or undiluted must specify the quantity required, must not be acted on more than once, or more than 7 days after date borne, and, unless issued under N.H.I. must be kept for two years
- (iii) Articles made with I M S on prescription *not* issued under N.H.I. must be entered in Prescription Book with name of person for whom prescription is written and person by whom signed. Prescriptions according to formulae given in any recognised book of reference may be quoted by the recognised short title.
- (iv) Not more than 1 pint of I M S alone, or diluted, or as an ingredient may be supplied at one time to any one person
- (v) Containers to be labelled

**SECOND SCHEDULE TO REGULATIONS** includes **collodions, liniments, tinctures** (*B.P.* and *B.P.C.*), etc., for external use only, **dry extracts**, preparations in the *N.I.F.* and *R.P.U. Formulary*, and **varnishes**, etc.

**NOTICE No. 55 (WHITE COLOUR)**—Applicable to doctors, dentists, veterinary surgeons, hospitals, and nursing homes

1. Medical men, etc., may obtain authority to receive I M S

2. I M S (95% Ethyl Alcohol denatured with 5% Wood Naphtha) may be had in various strengths, including a strength corresponding to absolute Alcohol

3. From a methylator not less than 5 gallons, or from an authorised wholesale or dispensing chemist not more than 1 gallon, may be obtained at one time, and official requisition must be sent

4. Without authority he may obtain  $\frac{1}{2}$  gallon from a chemist

5. I M S may be used for dispensing or be used without admixture for any medical, etc., purposes *only*

6. Must be labelled "For external use," or "Not to be taken," or words to that effect

Only 1 pint may be dispensed by a medical man, etc., either alone or as an ingredient, at one time for any one person

**French Polish or Finish (Spirit Varnish).**

Industrial M.S. may be used in making for sale (a) Mixtures containing not less than 8 ounces of resin (or 6 ounces of commercial shellac) to the gallon, (b) hot lacquers, irrespective of the proportion of resin (if not less than 3 ounces).

Mineralised M.S. may be used in making **Finish** for which the minimum of 3 ounces of gum resin is required

Mixtures (except hot lacquers) containing 3 ounces or more but less than 8 ounces (or 6 ounces if the resin is commercial shellac) to the gallon, must, if for sale, be made with I M S (Purified)

## ALLIUM

### *B.P.C.*

**Dose.**— $\frac{1}{2}$  to 2 drachms (2 to 8 g)

The fresh bulb of *Allium sativum* (*Liliaceæ*)

**Uses.** Preparations have been given in pulmonary phthisis, bronchiectasis, gangrene of the lung, and whooping cough.

**LARYNGEAL TUBERCULOSIS** has been treated by  $\frac{1}{2}$  to 1 drachm, 2 or 3 times a day, of the juice, with Tinct. Lavand. Co. and Syrup Simplex, also gargle or spray (or combined), accompanied by

poultice (or blister) of pulped garlic externally—latter also to tuberculous ulcers. Fresh juice is not so severe in action as the pulped garlic. The juice should never be applied to broken surfaces. Lengthy application of poultices (3 to 4 weeks with changes) may be required, but effect should first be tried for a few hours, as some are more susceptible than others. It was held by W. C. Minchin, who advocated the treatment, that allyl sulphide is specific in all tuberculous lesions in accessible situations, or in those which can be rendered accessible, and that every case of tuberculous disease in the leg, foot, arm, hand, testicle, etc., gets well under it.

For lupus, apply the fresh juice at night and allow to dry, wash off in morning and apply a bland ointment.

SUPPURATION OF WOUNDS may be controlled by *Succus Allii* diluted with 3 or 4 parts of water, a 1 in 10 dilution being used later when the suppuration is definitely controlled.

Rectal injections of the juice diluted with 3 parts of water have been used successfully in the treatment of duodenal ulcers. An inhalation of fresh garlic juice is also useful in pulmonary tuberculosis. The following solution may be used.—fresh garlic juice 56, alcohol (90%) 7, oil of *Eucalyptus citriodora* (Bayard) 1. 4 ounces is sufficient for 3 weeks' treatment of pulmonary tuberculosis. The juice is *fresh* and *not filtered*. Patient to use the inhalation in a respirator at least 1 hour night and morning. Capsules of allyl sulphide, 2 minims, can be used in addition if practicable.

**Emplastrum Allii.** Fresh garlic *q s*, pulped, 2 lb., to this add  $\frac{1}{2}$  lb. lard warmed to a cream, and mix thoroughly. Spread on thin butter-muslin and apply to the part, changing the dressing about every 24 hours.

### **Succus Allii (B.P.C.)**

*Dose.*— $\frac{1}{2}$  to 1 drachm (2 to 4 ml.)

The expressed juice preserved by the addition of alcohol.

### **Syrupus Allii (B.P.C.)**

*Dose.*— $\frac{1}{2}$  to 2 drachms (2 to 8 ml.)

Contains about 18% *v/v* of the juice.

**Allisatin** (*Sandoz, London, Brooks & Warburton, London*) Tablets of garlic and activated charcoal for intestinal affections, etc.

**Allium Cepa**, the ordinary onion, is of less strength than *Allium sativum*. *Hydrarthrosis* has been cured by placing the fleshy scales of the onion round the joint and keeping in place with a bandage.

**Allium Porrium.** The common leek also contains allyl sulphide.

**Oleum Allii Essentiale.** This oil is excreted through the lungs and skin—not apparently by the kidney. Its principal constituent is usually taken to be allyl sulphide. Stimulant, expectorant and stomachic. In chronic bronchitis, pneumonia, also in cholera and tuberculosis. *Dose* of either the natural oil or allyl sulphide,  $\frac{1}{2}$  to 2 minims, in capsules.  $\frac{1}{2}$  minim of allyl sulphide per kilo weight may be taken as lethal dose.

### **Allylis Sulphidum (B.P.C.)** ( $C_3H_5)_2S = 114.1$ .

*Dose.*— $\frac{1}{2}$  to 2 minims (0.03 to 0.12 ml.)

A colourless or yellowish oil with a garlic-like odour. B.p. about 138°, sp. gr. 0.890 to 0.900.

## ALOE

*B.P., U.S.P. XI.*

**Dose.**—2 to 5 grains (0.12 to 0.3 g.). *U.S.P. XI* average dose 4 gr.

Aloes is obtained by evaporating the juice which drains from the cut leaves of *A. chinensis*, *A. Perryi* and other species (*Liliaceæ*), known commercially as Cape, Curaçao, Socotrine or Zanzibar Aloes. Aloe (*Fr. Cx*, *P. Ital. V* and *F.E. VIII* (*Acibar*) and *P. Jap*) is from various species. *P. Helv. V* and *P. Belg. IV* specify *A. ferox*. *P. Dan.* includes *A. ferox* and other species. The Cape variety of aloes (from *A. ferox*) is of vitreous fracture, and characteristic odour, and mostly used for veterinary purposes. It contains as much as 10% of crystallisable aloins. Curaçao aloes may contain up to 30%.

**Uses.** Aloes and aloin act chiefly on the lower bowel. They are employed with soap and with iron and with strychnine in the treatment of habitual constipation.

Aloes, in dose of 10 grains a day, is very unsafe for pregnant women—very likely to produce abortion.—*Pharm. J.*, ii/1924, 343

**Decoctum Aloes Compositum (B.P.C.)**

**Dose**— $\frac{1}{2}$  to 2 ounces (15 to 60 ml)

A 1% solution of aloes, with myrrh, potassium carbonate, liquorice and compound tincture of cardamom. A purgative and emmenagogue.

**Decoctum Aloes Compositum Concentratum (B.P.C.)**

**Dose**—1 to 4 drachms (4 to 16 ml).

Diluted with 3 parts of water it yields a preparation of about the same strength as compound decoction of aloes.

**Extractum Aloes (B.P.C.)**

**Dose**—1 to 4 grains (0.06 to 0.25 g.)

The dried aqueous extractive.

**Glycerinum Aloes.**

Evaporate tincture of aloes 6 to 3, gradually adding glycerin 30. Pigment for bed sores and anal fissures.

**Pilula Aloes (B.P.)**

**Dose**—4 to 8 grains (0.25 to 0.5 g.)

Contains aloes 58%, and hard soap, 29%.

**Pilulae Aloes (U.S.P. XI).** *Average dose*—2 pills.

Each pill contains 2 grains of aloes and 2 grains of hard soap.

**Pilula Aloes et Asafœtidæ (B.P.).**

**Dose.**—4 to 8 grains (0.25 to 0.5 g.).

Contains 30% each of aloes, asafœtida and hard soap.

[P.] **Pilula Aloes, Cascaræ et Hyoscyami.**

**Dose**—4 to 8 grains (0.25 to 0.5 g.)

Extract of aloes, extract of cascara and extract of hyoscyamus, equal parts.

**Pilula Aloes et Ferri (B.P.).**

**Dose.**—4 to 8 grains (0.25 to 0.5 g.)

Contains exsiccated ferrous sulphate 10%, and aloes 20%, with cinnamon, cardamom and ginger.

**Pilulæ Aloes et Myrrhæ (B P C)** *Syn* PILULÆ RUFI*Dose*.—1 or 2 pills

Contain aloes 2 gr. and myrrh 1 gr.

**[P1 81] Pilulæ Aloes et Nucis Vomicae (B P C)***Dose*.—1 pill.Contain aloes 2 gr., dry extract of nux vomica  $\frac{1}{4}$  gr., and dry extract of belladonna  $\frac{1}{16}$  gr.**Pilula Triplex.** *Dose*—1 to 3 pillsExtract of aloes 2 gr., podophyllin  $\frac{1}{4}$  gr., pill of mercury 1 gr. Cathartic with particular action on the liver**Pulvis Aloes et Canellæ (B P C.)** *Syn* HIFRA PICRA.*Dose*.—3 to 10 grains (0.2 to 0.6 g)

Aloes 4, canella 1

Much used as a domestic emmenagogue

**Tinctura Aloes (B P C.)***Dose*.— $\frac{1}{2}$  to 2 drachms (2 to 8 ml). Aloes 1 in 40, and liquid extract of liquorice

Tampons saturated with this give relief in pruritus vulvæ

**Tinctura Aloes Composita (B P C.)***Dose*.—1 to 2 drachms (4 to 8 ml).

Aloes, about 1 in 30, with gentian, rhubarb and ginger

**Tinctura Aloes et Myrrhæ (B P C)** *Syn* ELIXIR PROPRIE-

FATIS

*Dose*.—1 to 2 drachms (4 to 8 ml)

Aloes about 1 in 10, with saffron, in tincture of myrrh

**Aperitive Elixir** *Dose*— $\frac{1}{2}$  to 1 drachm (2 to 4 ml)

Tincture of aloes 2, tincture of myrrh 2, tincture of saffron 1

**[P1] Dewees' Emmenagogue Mixture (Hare)***Dose*.— $\frac{1}{4}$  ounce thrice daily

Tincture of aloes 8, tincture of ferric chloride 6, tincture of cantharides 2, ammoniated tincture of guaiacum 3, syrup to 90 Largely employed in the U S in functional and organic amenorrhœa

**[P1] Tinctura Antiperiodica (B.P.C)** *Syn* WARBURG'S TINCTURE*Dose*.—1 to 4 drachms (4 to 16 ml)

Contains aloes 1 in 40, quinine sulphate 1 in 50, with opium (0.03%) and 15 other drugs

**Vinum Aloes (B P.C.)***Dose*.—1 to 2 drachms (4 to 8 ml)

Aloes about 1 in 30, with cardamom, in sherry-type wine

**Aloinum (B P, U.S.P. XI).***Dose*.— $\frac{1}{2}$  to 2 grains (0.03 to 0.12 g).  $\frac{1}{4}$  grain may be considered an aperient, and 1 grain a full purgative dose The former is U.S.P. XI average dose.A mixture of crystalline principles from aloes Usually obtained from Curaçao aloes and then contains approximately equal proportions of barbaloin (C<sub>21</sub>H<sub>20</sub>O<sub>9</sub>) and isobarbaloin.**Soluble** about 1 in 130 of water, 1 in 20 of alcohol 90%. Almost insoluble in ether, chloroform and benzene.

Administered in a pill with hard soap Assuming aloes to

contain 25% of aloin, it follows that  $\frac{1}{4}$  grain of the latter is equivalent in activity to 1 grain of aloes.

Has been tried as *hypodermic purgative*— $\frac{1}{2}$  grain in warm water 30 minims, but it is not always satisfactory

[P 81] **Pilulæ Aloini Compositæ** (B.P.C.) Syn. ANDREW CLARK'S LIVER PILLS

Dose —1 pill

Contain  $\frac{1}{2}$  gr. each of aloin, dry extract of nux vomica, exsiccated ferrous sulphate, myrrh and hard soap.

[P 81] **Pilulæ Aloini et Podophyllini Compositæ** (B.P.C.)

Dose —1 to 4 pills.

Aloin  $\frac{1}{10}$  gr., jalap resin  $\frac{1}{10}$  gr. and resin of podophyllum  $\frac{1}{8}$  gr., with oleoresin of capsicum and dry extracts of nux vomica and hyoscyamus.

[P 81] **Pilulæ Aloini et Strychninæ Compositæ** (B.P.C.).

Dose —1 or 2 pills

Aloin  $\frac{1}{8}$  gr., strychnine  $\frac{1}{10}$  gr with dry extract of belladonna and powdered ipecacuanha

[P 81] **Pilulæ Phenolphthaleini Compositæ** (B.P.C.) Syn PILULÆ PHENALOINI

Dose —1 or 2 pills

Aloin  $\frac{1}{4}$  gr., phenolphthalein  $\frac{1}{2}$  gr, strychnine  $\frac{1}{10}$  gr, dry extract of belladonna  $\frac{1}{12}$  gr, powdered ipecacuanha  $\frac{1}{15}$  gr

**Suppositoria Aloes** (Fr. C.x) Aloes 0.5 g, oil of theobroma 2.5 g

**Tabellæ Aloini** (B.P.C.) contain  $\frac{1}{2}$  gr. (0.03 g.).

[P 81] **Tabellæ Aloini Compositæ** (B.P.C.)

Dose.—1 or 2 tablets

Aloin  $\frac{1}{4}$  gr., powdered ipecacuanha  $\frac{1}{4}$  gr. and dry extract of nux vomica  $\frac{1}{4}$  gr

[P 81] **Alphen Pill** (Parke, Davis, London) Aloin, phenolphthalein, ipecacuanha, strychnine and extract of belladonna Dose —1 to 3 pills at bedtime

[P 81] **Asbic Pills** (Lilly, London) Aloin  $\frac{1}{4}$  gr, strychnine  $\frac{1}{10}$  gr, extract of belladonna leaves  $\frac{1}{4}$  gr, ipecacuanha  $\frac{1}{10}$  gr, calomel  $\frac{1}{4}$  gr

[P 81] **Lapactic Pills** (Sharp & Dohme, London) Aloin  $\frac{1}{4}$  gr, strychnine  $\frac{1}{10}$  gr, extract of belladonna  $\frac{1}{4}$  gr, powdered ipecacuanha  $\frac{1}{10}$  gr

## ALUMINIUM

Al = 26.97

**Pharmacology.** The soluble salts are gastro-intestinal irritants in large doses but do not cause chronic poisoning. When injected a slow toxic action occurs with fatty degeneration of liver and kidneys.

The use of aluminium cooking vessels is generally considered to be innocuous, although occasional cases of chronic malaise, possibly due to idiosyncrasy, have been reported, which cleared up on ceasing the use of aluminium utensils

The physiological action of aluminium compounds is discussed, the action is on the blood system and is observed only when injected. Ordinary amounts

have no action by the mouth, and aluminium in the diet in small amounts is harmless. The relief of pain attending the discontinuance of aluminium cooking vessels is due to psychological forces.—J H Burn, *Analyst*, 1932, 428

There is no convincing evidence that aluminium in the amounts in which it is likely to be consumed as a result of using aluminium utensils has a harmful effect upon the ordinary consumer. It is possible that there may be individuals who are susceptible to even such small doses of aluminium as may be derived from aluminium utensils, but evidence of this is inconclusive.—G. W. Monier-Williams, *Rep publ Hlth Med. Subj., Lond*, No. 78, 1935

**Alumen (B.P.).** *Syn.* ALUMEN PURIFICATUM, PURIFIED ALUM.

*Dose.*—5 to 10 grains (0.3 to 0.6 g.).

May be either potassium aluminium sulphate (potash alum),  $KAl(SO_4)_2 \cdot 12H_2O = 474.4$ , or ammonium aluminium sulphate (ammonia alum),  $NH_4Al(SO_4)_2 \cdot 12H_2O = 453.3$ . *U.S.P. XI, P. Helv. V and P. Dan.* have potash alum only. In colourless crystals or white powder with sweetish astringent taste

**Soluble** 1 in 10 of water (potash alum), 1 in 8 (ammonia alum), and 1 in 3 of glycerin, insoluble in alcohol.

**Uses.** As an astringent for local application, solutions of  $\frac{1}{4}$  to 1% or stronger may be used in stomatitis, pharyngitis, leucorrhœa, gonorrhœa, hyperhidrosis and weeping eczema. The solution may be used as a hæmostatic, for example, after tooth extraction. Stronger solutions harden the epidermis and are useful in treating soft corns. Ulcers on the lips may be cured by touching with a crystal of alum. As a mouth-wash its solution is possibly not desirable, since destruction of the teeth may occur unless it be quickly removed by rinsing. Internally alum is astringent in small doses and emetic in larger doses such as  $\frac{1}{4}$  to 1 teaspoonful, but is rarely given to induce emesis except in bronchitis, spasmodic croup and whooping cough in children. Whooping cough has also been treated with 1 to 2 dr doses of 2% solution at 2-hourly intervals in conjunction with adequate doses of chloral hydrate. Is also of considerable value in the treatment of lead colic.

**Aqua Hæmostatica (P. Ital. V, P. Belg. IV)** *Syn.* ACQUA DEL PAGLIARI

Alum (potash) 80, tincture of benzoin 10, benzoic acid 2, water to 1000. Filtered after allowing to deposit. Pollacci's modification contains 10% of sodium chloride

**Collyrium Aluminis (B.P.C.).** 1% w/v

**Gargarisma Aluminis (B.P.C.)** Glycerin of alum, 1 in 8, with acid infusion of roses.

**Glycerinum Aluminis (B.P.).**

Potash alum, 13% w/v in water and glycerin. An astringent in chronic pharyngitis; is less disagreeable than tannic acid.

**Injectio Aluminis (L H)** for vaginal use. 60 grains in 1 pint.

**Injectio Aluminis et Zinci (St. T H.).**

Alum 2 parts, zinc sulphate 1 part. Powder and mix

One or two teaspoonfuls dissolved in 1 pint of warm water for vaginal injection.

**Pessus Aluminis (B.P.C.)** contains 5 gr. (0.3 g.)

**Points of Alum** mounted in wooden cases are prepared for ophthalmic and other uses.

**Pulvis pro Pedibus (P. Helv. V)**

Potash alum 15, talc 85, in fine powder. For tender feet. Another useful form of foot powder is talc 2, boric acid 2, orris 1, zinc oleate 1

**Solvellæ Aluminis** (*B.P.C.*) contain 10 gr (0.6 g.)

**Alumen Chromicum** (*B.P.C.*)  $\text{KCr}(\text{SO}_4)_2 \cdot 12\text{H}_2\text{O} = 499.4$ .

Large violet crystals giving a violet aqueous solution which becomes green on heating to  $60^\circ$  to  $80^\circ$ , returning to the original colour on prolonged standing.

**Soluble** 1 in 7 of water; insoluble in alcohol 90%. Used commercially in tanning and as a mordant, also for hardening gelatin in photographic materials

**Alumen Exsiccatum** (*B.P.C.*, *P. Helv. V*, *U.S.P. XI*) *Syn.* ALUM USTUM, BURNT ALUM Made by heating potash alum until it has lost 45 to 46% of its weight. *U.S.* makes from potash or ammonia alum.

**Soluble** slowly and completely 1 in 20 of water. If dried above  $200^\circ$  the product will not dissolve completely owing to formation of oxysulphate

Is a powerful astringent useful as a dressing for old ulcers and sores. Also used for preserving skins

**Alumen Ferricum** (*B.P.C.*) *Syn.* IRON ALUM, FERRIC AMMONIUM SULPHATE.  $\text{NH}_4\text{Fe}(\text{SO}_4)_2 \cdot 12\text{H}_2\text{O} = 482.2$ .

**Dose.**—5 to 10 grains (0.3 to 0.6 g.) Amethyst coloured efflorescent crystals, of astringent taste. **Soluble** 1 in 3 of water (best with a little sulphuric acid added), insoluble in alcohol. Internally to arrest hæmorrhage, also as an astringent gargle ( $2^\circ$ ), throat spray or pigment ( $8^\circ$ )

**Aluminii Acetas.**  $\text{Al}_2(\text{C}_2\text{H}_3\text{O}_2)_6$

A gummy mass soluble in water, obtained by interaction of lead acetate and aluminium sulphate

**Aluminii Subacetat.**  $\text{Al}_2\text{O}_3 \cdot 4\text{C}_2\text{H}_3\text{O}_2 \cdot 4\text{H}_2\text{O}$  *P. Dan.* gives the formula  $\text{Al}(\text{OH})(\text{CH}_3\text{COO})_2$

A white powder sparingly soluble in water obtained by heating a solution of the normal acetate

Is used as a desiccant and deodorant in powder or with glycerin. For ophthalmia neonatorum a 10% ointment has been used, applied between the lids every hour, in place of silver nitrate drops

**HÆMORRHAGE, UTERINE AND POST-PARTUM** 2 to 3% solution of aluminium acetate used, never failed to arrest hæmorrhage from inertia of uterus at childbirth — *Per Prescriber*, 1923, 33

**OXYURIASIS** As an anthelmintic aluminium subacetate has been used in treatment of oxyuriasis. **Dose** for an adult 1 g. 3 times daily for three days, for children 0.5 g. twice daily—preceded in each case by a dose of calomel — *W. T. Schmidt, per Trop. Med. (Hyg.)*, 1923, 146

**VAGINAL DISCHARGE** After cleaning the vagina and cervix with hydrogen peroxide, a teaspoonful of granulated aluminium acetate (powder will not do, since it clots) is placed near the cervix and the vagina closed with a dry tampon, which is removed some hours later, this is done twice a week. After the second application there is usually a disappearance of the evil-smelling discharge — *R. Kuhn, Lancet*, 1/1936, 691

**Lenicet Ointment** (*Rudolph-Riddell, London*). Polymerised aluminium acetate 5%, anhydrous wool fat 10%, white soft paraffin 85%. In dermatitis, eczema, burns, etc. [**P1**] **Lenirenin Belladonna Ointment** is composed of Lenicet, adrenine, local anesthetics and 1% extract of belladonna. For hæmorrhoids, tenesmus, pruritus ani, etc. Also available as suppositories

**Liquor Aluminii Acetas** (*B.P.C.*, *P.G. VI*, *P. Austr.*, *P. Jap.*). *Syn.* LIQUOR ALUMINII ACETICUS, BUROW'S SOLUTION (Burow's



Solution, *P. Belg. IV*, is *Liquor Aluminii Aceto-Tartratis*, similar to *P. Helv. V*). A solution containing a basic aluminium acetate

Is much used on the Continent in place of boric lotion for moist fomentations in cutaneous crysipelas and other dermatoses. Gauze soaked in the solution may be used as a dressing for suppurating wounds. Diluted with twice its volume of water it is used as an antiseptic astringent lotion, and diluted 1 with 4 or more of orange-flower water it forms a pleasant mouth-wash.

A 1 in 8 dilution forms an effective substitute for Calamine Lotion, and in some cases may produce better and quicker therapeutic result.—R M B MacKenna, *Brit med. J.*, 1/1932, 78

*Note*.—Burow's Solution (*P. Ned V*) is made by interaction between potash alum and basic lead acetate solution, and contains some lead sulphate (0.6%) in solution and some undissolved. It contains only 1% approx of basic aluminium acetate.

[P1] **Solution de Burow avec Précipité** (*P. Belg IV*) Potash alum 10, lead acetate 50, water 940. The salts are dissolved in half the water and mixed.

**Aluminii Aceto-Tartras.** *Syn* ALSOL

Colourless crystals, scales, or crystalline powder, obtained by dissolving aluminium hydroxide in a mixture of acetic and tartaric acids.

Soluble 1 in 2 of water.

An astringent and antiseptic employed in 1 or 2% solution as mouth wash and gargle. Also for wound treatment—the same strength.

**Aluminium aceticum-tartaricum siccum** (*P. Helv. V*) is made by evaporating the solution below, adding a little acetic acid during the process.

**Liquor Aluminii Aceto-Tartratis.** *Syn* ALUMINIUM ACETIO-TARTARICUM SOLUTUM (*P. Helv V*)

Dissolve aluminium sulphate 30 in warm water 135, cool and add, with stirring, calcium carbonate 13, and then acetic acid (30%) 36, allow to stand 3 days with occasional shaking, filter off the solution and add to every 100 of filtrate tartaric acid 4½.

Sp. gr. 1.057 to 1.063. Contains about 10% of aluminium aceto-tartrate. According to *P. Helv V* this is to be supplied when Burow's solution is ordered.

*PG VI* contains 45% of aluminium aceto-tartrate, and is prepared by dissolving tartaric acid 15 in aluminium acetate solution 500, evaporating on the water bath to 114 and adding acetic acid 6. Filter after standing in stoppered bottle, protected from light. Sp. gr. 1.26 approx.

Stomatitis may be treated by frequent rinsing of the mouth with this solution and by using salol as a paste to the parts.

**Liquor Aluminii Formatis.** This may be prepared by precipitating the hydroxide from 630 of aluminium sulphate crystals, and dissolving in 1152 of 25% formic acid. Thus made, it contains the equivalent approximately of ½ its weight of aluminium formate taken as  $Al_2(HCOO)_4$ . Other formulæ have been given for aluminium formate. Employed like the foregoing as a gargle, diluted 1 to 3% with water.

**Aluminii Chloridum** (*B.P.C.*)  $AlCl_3 \cdot 6H_2O$  = 241.4

*Dose*.—2 to 4 grains (0.12 to 0.25 g.) May be administered in solution or as pills containing 2 gr.

A white, amorphous deliquescent powder. **Soluble** 2 in 1 of water, 1 in 4 of alcohol and in glycerin. Has been found of distinct service in locomotor ataxy; relieves the lightning pains.

**Liquor Aluminii Chloridi.** Dissolve aluminium chloride ( $+6\text{H}_2\text{O}$ ) 20, in water to produce 34 by volume = 42.5% by weight Sp gr 1.35.

**Aluminii Chloras.**  $\text{Al}(\text{ClO}_3)_3$  - 277.3

Deliquescent crystals containing either 6 or 9  $\text{H}_2\text{O}$

A 25% solution may be prescribed. Thus further diluted 1 to 25 forms a 1% mouth wash or spray in throat affections, and is a prophylactic against infection. A 20% solution in water or glycerin has been used on tampons for leucorrhœa or cervical catarrh.

**Aluminii Hydroxidum (B P C)**  $\text{Al}(\text{OH})_3$  = 78.0

*Dose* — 5 to 10 grains (0.3 to 0.6 g.)

Prepared by pouring hot potash alum solution into a hot solution of sodium carbonate. A white, odourless, tasteless, amorphous powder, insoluble in water, soluble in caustic alkali solutions. For the treatment of flatulence, hyperacidity, pyrosis and allied gastric disturbances.

**Alocol** (*Wander, London*) Colloidal aluminium hydroxide in powder, or tablets containing 0.5 g. *Dose* — 2 tablets to be dissolved in the mouth  $\frac{1}{2}$  hour before and after each meal.

**Collumina** (*Etans, Sons, Lescuyer & Webb, Liverpool*) Colloidal aluminium hydroxide for the treatment of gastric inefficiency and abnormal acidity of the stomach.

**Hydronal** (*Bayer Products, London*) Aluminium hydroxide with a strong peptisation action. Supplied in  $7\frac{1}{2}$  gr. tablets.

**Aluminii Sulphas (B P C).** *Syn* ALUMINIUM TRISULPHATE  $\text{Al}_2(\text{SO}_4)_3 \cdot 16\text{H}_2\text{O}$  - 630.4 *P. Helv. V* and *P. Dan.* have  $18\text{H}_2\text{O}$   
*Dose* — 2 to 5 grains (0.12 to 0.3 g.)

White crystalline powder or lumps made by dissolving freshly precipitated aluminium hydroxide in sulphuric acid. **Soluble** 1 in 1 of water nearly, **insoluble** in alcohol.

**Incompatible** with alkalis and alkaline carbonates.

**Uses.** Similar to alum but more astringent. A saturated solution has been used as a mild caustic for enlarged tonsils and nasal polypus. 5 to 10% solutions may be applied locally to ulcers. Wrinkles may be treated with the 1 in 50 solution.

**Kaolinum (B P)** *Syn and Prop Names* BOLUS ALBA (*P. G. VI, P. Jap., P. Helv. V, P. Dan.*), BOL. BLANC (*P. Belg. IV*), CHINA CLAY, KAYLENF (*Kaylene Ltd., London*) OSMO KAOLIN (*Morson, London, Allen & Hanbury's, London*) and COLLOSOL KAOLIN (*Crookes' Laboratories, London*) are brands of colloidal kaolin.

*Dose* —  $\frac{1}{2}$  to 2 ounces (15 to 60 g.), with water or milk. Best on empty stomach.

Native white, hydrated aluminium silicate, purified by elutriation from sandy matter. It is a soft whitish powder.

**Insoluble** in all ordinary solvents and in mineral acids.

**Uses.** Kaolin acts as a protective of the mucosa of the stomach and intestines, and is given as a substitute for bismuth carbonate in gastric and intestinal affections. It does not constipate like bismuth. Is superior to bismuth in that it is unaffected by the gastric juice. It also adsorbs toxins from the alimentary canal,

and is valuable in cholera, dysentery, bacillary diarrhœa, food poisoning and in diarrhœa of phthisis. Externally kaolin is a useful absorbent for irritation of the skin. It is unacted upon by most chemicals, hence used for making pills of silver nitrate, gold chloride and potassium permanganate (*see* Unguentum Kaolini). It is a useful filtering medium for clarifying liquids.

**ASIATIC CHOLERA.** A suspension of 800 g. of kaolin in a litre of water employed, 3 ounces being given every half-hour until vomiting and diarrhœa abated, then continued every hour and then every two hours up to 12 or 15 hours. Renders bacteria and toxins harmless by a process of adsorption—*Brit med J*, i/1926, 440.

More efficacious than injections of antiserum, iodine, or hypertonic saline. Mortality in cholera camps dropped from 44 to 3%. Tumblerful of emulsion containing 100 g. of kaolin in 250 ml cold boiled water given every half-hour or hour for 6 doses or more and continued for next few days with smaller dosage—*Indian med Gaz.*, Feb, 1926, 93.

**BURNS.** Spread a thick layer of kaolin powder daily on the burn, cover with gauze and a thin layer of zinc ointment—*Per Prescriber*, 1926, 336.

**FISTULÆ.** For protection of skin round gastric or intestinal fistulæ opening through the abdominal wall, kaolin is better than ointments—*Med. Annu*, 1931, 10.

**GASTRIC ULCER** 75 grains of a preparation containing aluminium silicate three times a day in milk satisfactory—*Lancet*, ii/1929, 681.

### **Cataplasma Kaolini (B.P.) Syn KAOLIN POULTICE.**

Kaolin 52.7%, boric acid 4.5%, with thymol, methyl salicylate, oil of peppermint and glycerin.

**Antiphlogistine** (*Denver Chemical Co., London*—for formula, *see* Vol. II), **Antithermogen** (*Hewlett, London*), **Caloplast** (*Allen & Hanburys, London*), **Sorbefacin** (*Christy, London*), and **Thermofuge** (*Parke, Davis, London*) are similar preparations used for relieving inflammation.

**PELVIC CELLULITIS OR PERITONITIS IN LABOUR.** Hot tampons of Cataplasma Kaolini with 5% Ext. Bellad. Virid., with hot vaginal douches, useful—*R. Nelson Ford, Brit med J*, ii/1930, 727.

### **Emulsio Paraffini Liquidi et Kaolini (B.P.C.).**

Dose— $\frac{1}{2}$  to 2 ounces (15 to 60 ml.).

Contains 25% v/v of liquid paraffin and about 80 gr. of kaolin per oz.

### **[P1 81] Mist. Kaolin. Sed. (N.I.F.)**

Kaolin 10 gr., tincture of chloroform and morphine 10 m., sodium bicarbonate 10 gr., water to  $\frac{1}{2}$  oz.

### **Unguentum Kaolini (B.P.C.). Syn KAOLIN MASS**

1 in 4 in a paraffin basis. Spread on lint and applied to abraded skin, it allays irritation. Also as pill excipient, *v. ante*.

**Carbokaylene** (*Kaylene Ltd., London*). Kaylene colloidal kaolin with activated charcoal. Dose—3 to 4 tablets three times daily half-hour before meals, for flatulence.

**Charkoalin** (*Allen & Hanburys, London*). Colloidal kaolin and activated charcoal in granules and tablets. For intestinal affections.

**Kaldrox** (*Petrolagar Laboratories Ltd., London*). Emulsoid of a 20% colloidal kaolin activated in a 2½% aluminium hydroxide gel. For gastric hyperacidity, intestinal putrefaction and diarrhœa.

**Kaomin** (*Lilly, London*). Powder containing bismuth subcarbonate 100, kaolin 280, magnesium hydroxide 60, sucrose 180, vegetable mucilage 20, vanillin 0.6. For colitis and gastric-intestinal diseases.

**Kaylene-Ol.** (*Kaylene Ltd., London*). Dose— $\frac{1}{2}$  ounce before meals. A preparation of kaolin with liquid paraffin for use as an evacuant and adsorbent.

**Lacto-Kaolin** (*Crookes' Laboratories, London*). Combination of Collosool kaolin and lactose for ulcerative colitis.

**Neutralon** (*Schering, London*) Synthetic aluminium sodium silicate. *Dose*—A teaspoonful in  $\frac{1}{2}$  glass of water 3 times daily. Astringent, antacid, adsorptive. Gastric hypersecretion, hyperchlorhydria and gastric and duodenal ulcer. [P1] **Belladonna-Neutralon** contains in addition 0.6% of extract of belladonna; for use where vagal irritability is present.

**Fullers' Earth** (*China Clay*) is a silicate similar to kaolin, containing traces of iron and magnesium.

Deaths of infants from tetanus when unsterilised fullers' earth has been applied to sores on navel and buttocks have been recorded. Warning should be given not to use it. Boric acid with zinc oxide and starch is safe.

**Cimolite** (*John Taylor, London*) is a special preparation of fullers' earth agreeably perfumed, for toilet and nursery use.

**Terra Alba** in commerce is variously kaolin, gypsum, burnt alum or magnesia, in preference the first.

**Talcum Purificatum** (*B.P.C., U.S.P. XI, P. Helv. V*). *Syn.* CRETA GALLICA PURIFICATA

A native hydrated magnesium silicate,  $Mg_3(Si_2O_5)_4(OH)_4$ , purified by treating with boiling dilute hydrochloric acid and washing free from acid. Venetian talc is from the Tyrol.

A soft white powder insoluble in acids and the ordinary solvents. Used in dusting powders to allay irritation and to prevent chafing. Also used as a lubricant for massaging, and in tablet making. Can be used as a filtering medium for clarifying liquids.

**French Chalk** is a harder silicate of magnesium.

**Soapstone.** A hard, massive variety of French chalk, consisting chiefly of magnesium hydrogen silicate,  $Mg_3H_2Si_4O_{11}$ .

**Steatite.** A hydrated magnesium silicate with some aluminium, iron, and lime, used as a furnace lining.

**Magnesium Silicate (Precipitated)** *Syn. and Prop. Name.* MAGNESIUM TRISILICATE, MAGSORBENT (*Kaylene Ltd., London*).

*Dose*—5 to 30 grains (0.3 to 2 g.).

A white amorphous magnesium silicate prepared by precipitation on mixing solutions of magnesium sulphate and sodium silicate. **Insoluble** in water. Interacts slowly with dilute mineral acids with formation of the magnesium salt of the acid and separation of colloidal silica.

**Uses.** Antacid and adsorbent. May prove preferable to other antacids and kaolin.

For a detailed account of its preparation and composition see Norman Glass, *Quart. J. Pharm.*, 1936, 445.

Certain hydrated silicates of magnesium possess strong antacid properties. The power of neutralising weak acids attains its maximum in the trisilicates. Synthetic hydrated trisilicate of magnesium exhibits powerful adsorbent qualities. At the saturation point for methylene blue it is seventeen times as active as colloidal kaolin (room temperature), and at body temperature the disparity is even greater. Its immediate adsorptive activity is considerable, but several days are required for saturation. The range of its adsorptive affinities covers a great variety of substances, including acid and basic dyes, alkaloids, bacterial toxins, putrefactive amines, and food poisons.—N. Mutch, *Brit. med. J.*, 1/1936, 148.

**PEPTIC ULCER.** 15 cases successfully treated by administration of hydrated magnesium trisilicate (Magsorbent), which on drying lost 10% of moisture and on ignition a further 15% of more closely combined water, in doses ranging from 7 to 28 grains (or 5 to 21 grains of the anhydrous substance) mid-way between each feed (feeds at first 2-hourly and later 3-hourly when pain was under control and occult blood tests negative), with 1 to 4 teaspoonfuls of an emulsion of paraffin in a watery dispersion of colloidal kaolin half an hour before each feed. The special features of the employment of a synthetic hydrated magnesium

**trisilicate** are: (1) the combination of antacid, antiseptic and antitoxic actions, (2) a sustained action whereby hydrochloric acid, destructive ferments and toxins can be removed continuously for several hours after administration of a single dose, (3) the possibility of a local therapy at the ulcer base, (4) freedom from the risk of inducing toxic alkalosis —N Mutch, *Brit med J*, 1/1936, 256

**Asbestos** is chemically a magnesium silicate

Pulmonary asbestosis in asbestos workers —*Brit med J*, 1/1930, 789; *Lancet*, i/1931, 1112 See also *ibid.*, ii/1931, 80, 306, 367, 1162.

Once asbestos bodies appear in the sputum the course is progressively downwards, and cessation of exposure to dust does not check advance —Wood and Gloyne, per *Med Annu.*, 1931, 56

**Diatomite** (*B P.C*) *Syn.* PURIFIED SILICEOUS EARTH, PURIFIED KIESELGUHR, TERRA SILICEA PURIFICATA (*U S P XI, P. Dan*)

Obtained from the siliceous skeletal remains of Diatomaceæ, large deposits being found in Scotland, Germany and elsewhere. The crude material is crushed, ignited, boiled with hydrochloric acid, washed and dried. Occurs as a bulky, white or pale buff odourless powder, **soluble** in alkalis, insoluble in acids except hydrofluoric. Used as an adsorbent dusting powder and as a filtering medium

**Sodium Silicate.** *Syn.* SOLUBLE GLASS, WATER GLASS

Is made by fusing silica, fine sand, or powdered flint, powdered coal and dried sodium carbonate mixed in powder, in an earthenware crucible, and pouring out the fused mass on to a stone slab to cool. This is pulverised and treated with boiling water to dissolve the soluble part. The solution is filtered and concentrated. Commercial solutions usually contain about 20% of silica and 10% of soda

SENILE PRURITUS well treated by intravenous injections of 1% sodium silicate, each injection representing 0.01 to 0.02 g. of the pure silicate. From 8 to 12 injections necessary, given at intervals of 2 or 3 days. *Brit med J Epit*, 1/1926, 64

SKIN DISORDERS, such as psoriasis, furunculosis, and acute weeping eczema, arteriosclerosis, tuberculosis of the lungs, stenosis of the cardiac valves, well treated with sodium silicate. It is best given intravenously, 1 ml. of 1% solution, on alternate days, up to 15 or 20 doses, but silica may also be administered hypodermically or *per os* —*Lancet*, ii/1925, 392

**Silantox** (*Silica Gel, London, Savory & Moore, London*) Colloidal silica. Used internally as an intestinal absorbent and externally as a dusting powder

**Silicosis.** The presence of silica in the lungs leads to fibrosis and predisposes to consumption

Industrial tuberculosis and factory ventilation, with special relation to inhalation of siliceous dusts —C A Winslow, *J Amer med Ass*, ii/1925, 968

Silicosis itself is not a very dangerous disease—it only causes shortness of breath and difficulty in breathing—but it becomes extremely dangerous and fatal when infected or contaminated with tubercle —*Lancet*, ii/1928, 202

For a summary of the silica content of normal and silicotic lungs and its bearing on the problem of silicosis see F S Fowweather, *J Soc chem Ind*, 1934, 713

## AMMONIUM

[P2] "*Ammonia*"

[B3] "*Ammonia—in substances not being solutions of ammonia or preparations containing solutions of ammonia; substances containing*

less than 5%, weight in weight, of ammonia ( $\text{NH}_3$ ); refrigerators; smelling bottles."

**Ammonii Carbonas** (*B P*, *U.S.P. XI*, *P. Helv. V*).

*Dose*.—5 to 10 grains (0.3 to 0.6 g.) *U.S.P. XI* average dose 5 grains

White masses with ammoniacal odour and alkaline taste, consisting of a variable mixture of ammonium bicarbonate ( $\text{NH}_4\text{HCO}_3 = 79.05$ ) and ammonium carbamate ( $\text{NH}_4\text{NH}_2\text{CO}_2 = 78.06$ )

*Soluble* 1 in 4 of water, 1 in 5 of glycerin. The carbamate portion is soluble in alcohol 90%

*Incompatible* with acids, iron salts and salts of alkaline earths

*For dispensing*, powdered ammonium carbonate is unsuitable since if the bottle is frequently opened ammonium bicarbonate is formed. A 1 in 8 solution has been found to be stable. It is best prepared by suspending translucent lumps, free from powder, in a muslin bag just below the surface of the water in a covered vessel

*Uses*.—Ammonium carbonate is stimulant, carminative and expectorant. Is excreted as urea and has a slight diuretic action. Does not increase alkalinity of blood or urine. Used as a stimulating expectorant in chronic bronchitis, broncho-pneumonia, especially of children, and in cardiac asthma. The solution is a useful application to insect bites and wasps' stings

**Liquor Ammonia Aromaticus** (*B P C*)

*Dose*— $\frac{1}{4}$  to 1 drachm (1 to 4 ml.)

Is prepared with ammonium carbonate, strong solution of ammonia and terpeneless oils of lemon and nutmeg and is of the same ammoniacal strength as the official spirit

It gives a clear mixture with distilled water as distinct from the *B P* spirit. It is not so pungent to the taste

**[P2] Liquor pro Spiritu Ammonia Aromatica.**

For dilution 1 with 3 of a mixture of alcohol (90%) 12 and water 1

Dissolve ammonium carbonate 4 oz. in water 20 oz. Add strong solution of ammonia 8 oz. then terpeneless nutmeg oil 54 m. and terpeneless lemon oil 13 m. in alcohol (90%) 10 oz.

May also be prepared for dilution 1 with 2 with the same alcohol mixture as for the "1 with 3" preparation above. In this case proceed as for the latter, but dissolve the ammonium carbonate in water 21  $\frac{1}{2}$  oz. and the oils in alcohol 90% 21  $\frac{1}{2}$  oz. This is clearer than the above

**Mistura Ammonia cum Senega** (*B P C*).

*Dose*.— $\frac{1}{2}$  to 1 ounce (15 to 30 ml.).

Contains 4 gr. of ammonium carbonate and 5 gr. of ammonium chloride with tincture of *ippecacuanha*, syrup of *tolu*, and infusion of *senega* to 1 oz.

**Spiritus Ammoniae Aromaticus (B.P.).** *Syn.* SPIRIT OF SAL VOLATILE.

*Dose.*—15 to 60 minims (1 to 4 ml.)

Ammonium carbonate dissolved in a mixture of strong solution of ammonia with a distillate of oil of lemon, oil of nutmeg, alcohol and water. Contains 2 1 to 2 4% *w/v* of  $\text{NH}_3$ .

**Spiritus Ammoniae Aromaticus (U.S.P. XI).**

*Average dose*—30 minims (2 ml)

Prepared by dissolving oils of lemon, lavender and nutmeg in alcohol, adding a solution of ammonium carbonate and ammonia water, and filtering after 24 hours. It contains more ammonium carbonate and less ammonia than the corresponding preparation of the *B.P.*

**Ammonii Bicarbonas (B.P.)**  $\text{NH}_4\text{HCO}_3 = 79.05$ .

*Dose*—5 to 10 grains (0.3 to 0.6 g.)

A white crystalline powder or white crystals volatilising slowly at room temperature. **Soluble** 1 in  $5\frac{1}{2}$  of water; insoluble in alcohol 90%.

Is formed from ammonium carbamate when ordinary ammonium carbonate is exposed to air, and has been suggested as a more stable compound for use instead of the carbonate, especially for preparing tablets and capsules.

[P2] **Liquor Ammoniae Fortis (B.P.).**

*Dose.*—3 to 6 minims (0.2 to 0.4 ml.).

Contains 32.5% *w/w*  $\text{NH}_3$ , sp. gr. 0.885 to 0.891. AQUA AMMONIAE FORTIOR (U.S.P. XI) contains 27 to 29% AMMONIAQUE OFFICINALE (*Fr. Cx.*) 20.18%. AMMONIACA LIQUIDA (*P. Ital. V, F.E. VIII*) is 20%; sp. gr. 0.925.

**Antidotes.** Stomach tube and emetic must *not* be used. Give well diluted vinegar freely, or copious drinks of orange or lemon juice. Keep patient lying down and warm. Demulcent drinks, olive oil. Morphine,  $\frac{1}{4}$  gr., hypodermically for pain. Tracheotomy may be necessary.

**Enema Ammoniae.** Strong solution of ammonia 1, water 160 (1 drachm to the pint).

Has been used in post-operative ileus and intestinal paresis. Its effect is enhanced by a dose of pituitary extract hypodermically given  $\frac{1}{2}$  hour previously.

**Linimentum Ammoniae (B.P.C.).**

Contains 25% *v/v* of solution of ammonia with oleic acid and liquid paraffin. Does not thicken on standing as is the case with liniments made with vegetable oils. Liniment of ammonia is usually supplied for hartshorn and oil.

[P2] **Liquor Ammoniae Domesticus (vel Detergens), Household Ammonia.**

Oleic acid 1, alcohol 1, mix and add strong solution of ammonia 7, distilled water 7; shake well. For use diluted as a detergent of the skin. In the bath 1 in 1000 to 2000 softens the water, also for general domestic purposes.

[P2] **Cloudy Ammonia** is made with tap water—for this the gravity of the preparation must not be too light, otherwise the lime salts constituting the "cloud" will settle down. The following is a suitable formula:—Dissolve castile soap 1.3 in water 60, and add strong solution of ammonia 27, lime water 0.6, and water to 100.

**Lotio Olei Amygdalæ Ammoniata (B.P.C.).**

*Syn.* LOTIO CRINALIS, ERASMUS WILSON'S HAIR LOTION.

Almond oil 1 in 8, strong solution of ammonia 1 in 8, with oil of rosemary, in alcohol 90%, and honey water.

For alopecia areata strong ammonia solution 1, chloroform 1, olive oil 1, spirit of rosemary to 8, is useful

[P2] **Liquor Ammonia Dilutus (B.P.).** *Syn.* LIQUOR AMMONIÆ, AQUA AMMONIÆ (U.S.P. XI), AMMONIA LIQUIDA (P. Ned. V), AMMONIUM HYDRICUM SOLUTUM (P. Helv. V).

Contains 10% w/w of  $\text{NH}_3$ . [P2] AMMONIAQUE DILUÉE (Fr. Cx) is about the same strength.

*Dose.*—10 to 20 minims (0.6 to 1.2 ml.).

*Hypodermically* 2 to 6 minims for collapse, or up to 36 minims for snake poisoning.

Internally it is stimulant, diuretic and diaphoretic. Used as a restorative by inhalation, it acts by reflex stimulation of heart and respiration.

In embolism large doses of ammonia, well diluted, tend to reduce the coagulability of the blood.—Whitla.

Ocular injury caused by inhalation of 10% ammonia.—I. Abramowicz, per *Prescriber*, 1926, 63.

**Ammonii Acetas (B.P.C.)**  $\text{CH}_3\cdot\text{COONH}_4 = 77.06$ .

*Dose*—10 to 30 grains (0.6 to 2 g.)

This salt is obtainable in white crystals, very soluble in water.

**Incompatible** with mineral acids, alkaline carbonates, potassium chlorate and dichromate, and with mercurous nitrate.

Serviceable in all fevers and in delirium tremens, one drachm every hour at first, reduced gradually

*Choice of a diuretic*—Ammonium, sodium and potassium acetate, citrates and tartrates increase osmosis and are diuretics by stimulating the convoluted tubes of the kidney. They draw water from the tissues into the blood stream, they do not irritate the kidneys and may be used even when the organs are acutely inflamed,—they should be well diluted. Useful to combine spirit of nitrous ether with them, which, owing to the ethyl nitrite contained in it, is a useful agent in causing dilatation of the different vessels of the kidney. The action of these drugs, *e.g.*, in renal dropsy, should be encouraged by sufficient doses of a watery aperient every day or other day, *e.g.*, compound jalap powder. —*Brit. med. J.*, 1/1911, 289.

**Liquor Ammonii Acetatis Fortis (B.P.).**

*Dose*—15 to 60 minims (1 to 4 ml.).

Prepared by neutralising glacial acetic acid with ammonium carbonate and a sufficient quantity of strong solution of ammonia, and diluting the product with distilled water. It contains 57.5% w/v of  $\text{C}_2\text{H}_7\text{O}_2\text{N}$  and has a pH of 7.0 to 8.0.

**Liquor Ammonii Acetatis Dilutus (B.P.).** *Syn.* LIQUOR AMMONII ACETATIS, SOLUTION OF AMMONIUM ACETATE.

*Dose.*— $\frac{1}{4}$  to 1 ounce (8 to 30 ml.).

Strong solution of ammonium acetate 1 part, distilled water to 8 parts. It contains 7.2% of  $\text{C}_2\text{H}_7\text{O}_2\text{N}$ .

Keep in lead-free stoppered bottles.



**Liquor Ammonii Acetatis (U.S.P. XI)***Average dose*— $\frac{1}{2}$  ounce (15 ml)

Prepared so as to yield a solution containing free acetic acid and carbon dioxide, and for dispensing purposes it is required to be freshly prepared. It is made by dissolving 5% of solid ammonium carbonate in dilute acetic acid (5.7 to 6.3%) or by mixing a 10% w/v solution of ammonium carbonate with a 32% v/v solution of acetic acid (36 to 37%) in water. *P. Helv. V* contains 15 to 16% Acetate d'Ammonium Dissous (*P. Cx*) contains 18.5 w/w.

**Liquor Ammoniaë Anisatus (B.P.C.)** *Syn.* SPIRITUS AMMONIAE ANISATUS

*Dose.*— $\frac{1}{4}$  to 1 drachm (1 to 4 ml)

Contains 16.67% v/v of dilute solution of ammonia with oil of anise in alcohol 90%. Several foreign pharmacopœias, *e.g.*, *P.G. VI*, give similar formulæ.

**Mistura Ammonii Acetatis Composita (B.P.C.)***Syn.* MISTURA DIAPHORETICA*Dose.*— $\frac{1}{2}$  to 1 ounce (15 to 30 ml.).

Potassium citrate 20 gr with strong solution of ammonium acetate, spirit of nitrous ether and spirit of chloroform in camphor water to 1 oz.

**Mist. Salin. (N.I.F.)** *Syn.* MIST DIAPHORETICA

Potassium citrate 10 gr, strong solution of ammonium acetate 8 m, concentrated solution of ethyl nitrite 2½ m (equivalent to spirit of nitrous ether 20 m), camphor water to ½ oz.

**[P1] Mistura Anti-Catarrhalis (Burney Yeo)**

Solution of ammonium acetate 3 dr, spirit of nitrous ether 1 dr, tincture of opium 10 m, ipecacuanha wine 5 m, camphor water to 1½ oz. To be taken at night. Assists action of skin and kidneys.

**Ammonii Citras (B.P.C.)**  $C_3H_4OH(COONH_4)_3, H_2O$  - 261.2

*Dose.*— $\frac{1}{2}$  to 1 drachm (2 to 4 g)

A deliquescent white powder tending to lose ammonia to form an acid salt. A mild expectorant and diuretic acting similarly to the acetate.

**Liquor Ammonii Citratis Dilutus (B.P.C.)** *Syn.* LIQUOR AMMONII CITRATIS.

*Dose*—2 to 6 drachms (8 to 24 ml)

Contains about 15% w/v of ammonium citrate. Keep in green bottles.

**Liquor Ammonii Citratis Fortis (B.P.C.)***Dose*— $\frac{1}{2}$  to 1½ drachms (2 to 6 ml).

Four times as strong as the above

**Ammonii Nitras (B.P.C.)**  $NH_4NO_3$  *Dose*—5 to 20 grains (0.3 to 1.2 g.). Occurs in colourless crystals, m.p. 165°. 7½ gr tablets, enteric coated, have been administered to render the urine acid. The fused salt is used for making nitrous oxide (*q.v.*)

Doses of 10 to 12 grains daily frequently maintain diuresis and diminish œdema in cardiac insufficiency, where other drugs fail. Disguise taste with syrup of orange—*P. Vallery-Radot* and *E. Gilbrin, Brit med J Epit*, ii/1932, 16.

**Hydroxylamine.**  $NH_2OH$  33.03. Its strong reducing and antiseptic properties suggest its use in tinea and psoriasis. Does not stain the skin. The HYDROCHLORIDE,  $NH_2OH \cdot HCl$  - 69.50, is freely soluble in water. Solution 1 in 1000 of equal parts of glycerin and alcohol, or ointment with *Adeps Lanæ*, successful in lupus, ringworm and parasitic syphilis. May produce smarting.

**AMPULLÆ****Ampoules**

Ampoules are glass containers for preparations intended for parenteral administration and contain only sufficient material for one dose. The *British Pharmacopœia* requires all solutions intended for injection (unless for intravenous injection) to contain an antiseptic equivalent in bactericidal activity to 0.5% of phenol, if more than one dose is dispensed in a single container. This requirement, therefore, does not apply to single dose ampoules.

The dispensing of sterile preparations in ampoules is by far the best method, since there is no possibility of the contents becoming infected and non-sterile during storage.

Ampoules vary in shape and their capacities range from 0.5 ml (8 minims) to 100 ml. (3½ fl ozs). The most frequent capacity is 1 ml. (15 minims).

They should be made from glass of high chemical resistance and when required for solutions of certain substances, such as alkaloidal salts, adrenaline, liquid extract of pituitary, insulin, etc., they must conform with the tests for the limit of alkalinity of glass as described in the *British Pharmacopœia*. This test requires ampoules, up to a capacity of 25 ml, to be filled with a standard acid solution of methyl red and then sealed and heated. To pass the test, there must be no change of colour of the methyl red solution from pink to a full yellow colour. This test would appear to need modification for as only the interior surface of the ampoule can yield alkali (if any) to the acid solution of methyl red, and as each ampoule is required to be *filled* with the test solution, it is obviously a much more severe test for a 1 ml. ampoule than for a 2.5 ml. ampoule.

When required for preparations liable to be affected by light, amber-coloured glass should be used.

Ampoules as received from the manufacturers are usually sealed. They should always be unsealed and thoroughly washed out with distilled water. It is not uncommon to find fine particles of glass in the sealed ampoules as received from the manufacturers. Great care should be taken to guard against such fragments remaining in the final preparation, the finished ampoules being carefully examined in a good light. The ampoules should be sterilised after washing, either in an autoclave at 115° for 30 minutes or in a hot air oven at 150° for one hour.

Ampoules may be filled on a small scale by means of a hypodermic syringe, and on a large scale by means of a burette fitted with a hypodermic needle, or by inverting the empty ampoules in the solution, placing under reduced pressure and then releasing the pressure, when the solution will be sucked into the ampoules. Sealing is done in the blow-pipe flame and it should be tested by placing the ampoules in some coloured solution, and then warming and cooling the latter, or by placing the ampoules immersed in the solution under reduced pressure and releasing the pressure.

The coloured solution will enter any ampoules which are improperly sealed and these should be rejected.

*Each ampoule should be individually labelled with the name and strength of its contents, such as 1 ml. = 0.02 g. Morph. Hydrochl*

Ampoules may also be used as containers for solid substances, such as neoarsphenamine, sodium citrate, sodium bicarbonate or iodophthalein required for the preparation of sterile solutions. Such solutions are made by adding sterilised water to the solid in the ampoule, dissolving, and using immediately. Special aseptic precautions must be taken with the preparation of these as it is rarely possible to heat and sterilise the final sealed container. The operation should be carried out in a special room which is supplied with filtered air, and precautions should be taken against infection from the hands and breath of the operator. It is advisable to test the powder for sterility before filling.

Special ampoules are used for powders. They have a wider neck than an ordinary ampoule and, as supplied by the manufacturers, the neck terminates in a funnel to facilitate filling with the powder. This funnel is then cut off and the ampoule sealed. It may be necessary in certain cases, such as neoarsphenamine, to replace the air with an inert gas to prevent oxidation during storage. This is done by leading the gas (nitrogen or carbon dioxide) into the ampoule through a glass capillary tube or hypodermic needle which is connected to the gas reservoir. The gas is allowed to pass into the ampoule for a few seconds and the ampoule is then quickly sealed.

It is customary to supply with ampoules containing solids an equal number of ampoules containing either sterilised distilled water or sterilised normal saline.

**Sterules** (*Martindale, London*) are ampoules containing sterile solutions, for hypodermic, intramuscular or intravenous injection, or dry powders for making solutions extemporaneously, or substances for inhalation. In the latter case the ampoule is encased in cotton wool and silk. It is broken between the fingers and the contents inhaled.

The **Ophthalmic Sterule** is inserted through an ejector, and its "breach," end is snapped off at the file mark. It is drawn further through the ejector, held horizontally, and the other end is broken off at the file mark. The "breach" end of the ejector is now covered with the index finger, and the soft part is pressed with the thumb and second finger to release a small quantity (sufficient for one application in eye work) of a sterile solution. The file marks are situated  $\frac{1}{4}$  inch from the ends of the "Sterule."

Solutions in ampoules for injection are issued also under other proprietary names, such as **Ampulique** (*Hewlett, London*), **Azoule** (*Allen & Hanburys, London*), **Glaseptic** (*Parke, Davis, London*), **Hypoloid** (*Burroughs Wellcome, London*), **G.L.** (*Glaxo Laboratories, London*), **Tubunic Ampoule Syringe** (*Hoffmann-La Roche, London*), consisting of a collapsible tube filled with the solution and fitted with a needle.

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## AMYGDALA AMARA

*B.P.C., U.S.P. XI, P. Helv. V.*

The dried ripe seeds of *Prunus communis* var. *amara*. Contains 50% of fixed oil and 3 to 4% of amygdalin, and yields 3 to 4% of essential oil.

**Antidotes.** Treat as for poisoning by hydrocyanic acid, see p. 65.

[P1 81] **Aqua Amygdalæ Amaræ** (I A) contains 0.1% of HCN

*Average dose* — 1 drachm

F. Norsk gives a "synthetic" bitter almond water, viz —

Oil of bitter almond 4, hydrocyanic acid (2%) 50, alcohol (90%) 146, distilled water 800. Contains 0.1% HCN

**Lotio Amygdalæ Amaræ** (B.P.C.) *Syn.* MISTURA AMYGDALÆ AMARÆ

Bitter almond 7½% w/v in water

**Oleum Amygdalæ** (B.P., P. Helv. V, P. Dan.) is expressed from the seeds of the bitter or the sweet almond. The content of oil in bitter almonds is about 50% and in sweet almonds about 45 to 50%. The residue from bitter almonds is utilised for the production of essential oil of bitter almond.

**Solubility.**—Almond oil dissolves in all proportions in chloroform, about 1 in 2½ of ether and slightly in alcohol 90%.

[P1 81] **Oleum Amygdalæ Amaræ** (B.P.C., U.S.P. XI)

*Syn.* OLEUM AMYGDALÆ ESSENTIALE

*Dose.*—½ to 1 minim (0.016 to 0.06 ml).

The natural oil may contain up to 10% of HCN but is adjusted to contain from 2 to 4%. It is stated that the presence of the HCN retards oxidation of the benzaldehyde to benzoic acid. The oil can also be distilled from apricot and peach kernels.

The glycoside amygdalin,  $C_{10}H_{11}NO_{11} \cdot 3H_2O \approx 511.2$ —crystals with slightly bitter taste, soluble in 12 parts of water—in the presence of the enzyme emulsin, a constituent of the seeds, takes up water on coming in contact with it, forming dextrose and benzaldehyde cyanohydrin,  $C_6H_5CH(OH)CN$  (P.G. VI). A similar body to amygdalin, possibly identical with it, is contained in cherry laurel leaves, from *Prunus Laurocerasus*.

Amygdalin is also contained in the bark of *Prunus serotina* (Virginian prune or wild cherry bark), and the same action occurs when this drug is bruised with water.

**Oleum Amygdalæ Amaræ Sine Acido Hydrocyanico** (B.P.C.) *Syn.* OLEUM AMYGDALÆ AMARÆ (S.A.P.)

*Dose* — ½ to 1 minim (0.016 to 0.06 ml).

Consists of the above essential oil freed from HCN by treatment with ferrous sulphate and calcium hydroxide, and redistillation. Contains not less than 95% w/w of benzaldehyde.

**Spiritus Amygdalæ Amaræ** (B.P.C.) *Syn.* ESSENCE OF BITTER ALMONDS

1 in 16

**Benzaldehydum** (B.P.C., P.G. VI, F.E. VIII, P. Jap. IV)  $C_6H_5CHO$  - 106.0.

*Dose* — ½ m. (0.03 ml)

A colourless or slightly yellow liquid, sp. gr. about 1.051, solidifying at about 26° and boiling at about 180°. Used as a flavouring agent in place of the natural oil of bitter almond.

**Amygdala Dulcis** (B.P.C.). *Syn.* SEMEN AMYGDALI DULCIS (P. Dan.).

The dried ripe seeds of *Prunus communis* var. *dulcis*. Contains fixed oil but no amygdalin.

**Lotio Rosæ** (B.P.C.) *Syn.* MILK OF ROSES. A perfumed emulsion of sweet almond, 1 in 10, with white beeswax and almond oil.

**Mistura Amygdalæ** (B.P.C.)

*Dose* — ½ to 1 ounce (15 to 30 ml)

Compound powder of almond 1 in 8 in water. A demulcent vehicle for cough mixtures and for suspending liquids not miscible with water.

**Pulvis Amygdalæ Compositus (B.P.C.).** A mixture of powdered sweet almond, sucrose and acacia

**Oleum Persicæ (B.P.C.).** *Syn.* PEACH OR APRICOT KERNEL OIL (or mixtures) Is obtained from the kernels of *Prunus Persica* (peach) or *Prunus Armeniaca* (apricot) The latter is used almost exclusively. The oil is used instead of almond oil in the culinary arts and for face creams, etc.

There is no pharmacological difference between this oil and the expressed oil of almonds

## AMYLUM

### B.P., U.S.P. XI

Maize starch, from *Zea Mays*, is the only variety official in B.P. '32 and U.S.P. XI, but B.P. Add admits also rice starch (*Oryza sativa*) Other common commercial varieties are obtained from wheat (*Triticum aestivum*) and potato (*Solanum tuberosum*) P. Helv. V includes arrowroot, rice, oat and wheat starches P. Dan. has arrowroot, potato and wheat Potato starch, by treatment with hydrochloric acid, yields **Amylum Solubile**. Soluble starch is readily soluble in hot water

**Cataplasma Amyli (B.P.C.).** Starch 10% boiled with water

**Cataplasma Amyli (St. J. H.).**

Boric acid 1 dr., starch 1 oz., cold water 2 oz., boiling water to 20 oz

One of the very safest remedies to apply to an inflamed, weeping or crusted surface and many cases of infantile eczema can be completely cured by its continued use alone —J. E. M. Wigley, *Practitioner*, 1935, 353

**Glycerinum Amyli (B.P.)**

Starch 8.5% w/w heated with water and glycerin at not over 140° until it gelatinises.

**Glyceritum Amyli (U.S.P. XI)**

Starch (maize) 1, water 2, glycerin 7, heated to 140° to 144°

**Tapioca Starch.** *Syn.* MANIHOT, MANIOCA OR MANDIOCA STARCH, from Brazil may form a commercial competitor of the varieties in use

Starch and its structure —Prof. Larg and co-workers, *Pharm. J.*, 11/1927, 398

**Maranta (B.P.C.).** *Syn.* ARROWROOT The starch from *M. arundinacea* (Marantaceæ). 1 tablespoonful to the pint of hot water produces a demulcent mucilage Many varieties of starch have been substituted for maranta, including that from the potato, sweet potato (*Ipomœa Batatas*), and *Curcuma*

**Mucilago Marantæ.**

Triturate arrowroot 6 dr. with water 2 oz. to make a smooth paste and make up with boiling water to 1 pint Heat until semi-transparent. Cool and add spirit of chloroform 2 dr

To suspend heavy medicaments this and a similar preparation of cornflour have been found useful It will suspend bismuth salts in a proportion as high as 1 drachm to the ounce.

**Lycopodium (B.P.C., P. Helv. V, P. Dan., U.S.P. XI)** The spores of the clubmoss, *Lycopodium clavatum* (Lycopodiaceæ).

*U.S.P. XI* requires not more than 0.75% of acid-insoluble ash. As a pill powder, also as a diluent for insufflations for the throat, nose, and ear, and as a dusting powder. Its use in quantitative microscopy is based on the presence of 94,000 spores per mg.

**Tinctura Lycopodii (B P C)**

*Dose*.— $\frac{1}{4}$  to 1 drachm (1 to 4 g). 1 in 10

To stop frequent micturition and irritation of the bladder.

## ANETHUM

(with ANISUM, ANTHEMIS, etc.)

**Anethum (B P)** *Syn.* DILL

Consists of the dried ripe fruits of *Anethum graveolens* Linn.

**Oleum Anethi (B P)**

*Dose* — 1 to 3 minims (0.06 to 0.2 ml)

Distilled from dill it is a yellow oil with odour resembling caraway. Sp. gr. 0.900 to 0.915. It contains not less than 43 to 63% *w/w* of carvone,  $C_{10}H_{14}O$

**Soluble** 1 in 1 of alcohol 90% and 1 in 10 of alcohol 80%

**Aqua Anethi Concentrata (B P)** is prepared with 2% *v/v* of oil of dill, and is approximately 40 times the strength of the distilled water

**Aqua Anethi Destillata (B P)** is prepared by distillation from dill.

**Anisum (B P C, P Helv. V, P Dan)** Anise (aniseed) is the dried ripe fruit of *Pimpinella Anisum* (Umbelliferae). Contains  $1\frac{1}{2}$  to  $3\frac{1}{2}$ % of volatile oil

**Aqua Anisi Concentrata (B P C)**

*Dose* — 5 to 15 minims (0.3 to 1 ml)

Contains 2% *v/v* of oil and is approximately 40 times the strength of the distilled water

**Aqua Anisi Destillata (B P C, U S P XI)** Distilled from anise, 1 in 10

**Syrupus Anisi (B P C)**

*Dose* —  $\frac{1}{4}$  to 1 drachm (2 to 4 ml)

Concentrated anise water 1, syrup to 8

**Anisi Stellatum (B P C)** *Syn.* STAR ANISE FRUIT, BADIANE

The ripe fruits of *Illicium verum* (Magnoliaceae), containing about 5% of volatile oil

**Oleum Anisi (B P, U S P XI)**

*Dose* — 1 to 3 minims (0.06 to 0.2 ml.).

Volatile oil from anise or from star anise, the latter source being used exclusively in this country. Colourless or yellowish oil congealing at not lower than 15° and melting again at not below 17°. Sp. gr. 0.980 to 0.994

**Elixir Anisi (B P C)** *Dose* —  $\frac{1}{4}$  to 2 drachms (2 to 8 ml)

Contains oils of anise, fennel and bitter almond (without HCN), in alcohol, syrup and water.

**Linctus Anisi (C X H)**

Oil of anise 1 m, chloroform 1 m, vinegar of squill 10 m, liquid extract of liquorice 10 m, mucilage of tragacanth to 1 dr

**Spiritus Anisi (B P C).** *Dose*.—5 to 20 minims (0.3 to 1.2 ml.) 1 in 10 in alcohol 90%. *U S P. XI* has the same strength in alcohol 95%.

**Eau de Botot.** Oil of anise 20, oil of peppermint 13, tincture of saffron 5, alcohol 70% to 1600. Some formulæ contain cinchona, rhatany, clove, etc

**Anetholum** (B.P.C.). *Syn.* *p*-METHOXYPROPENYL BENZENE.

$C_9H_9(OCH_3)C_6H_5$ , = 148.1.

*Dose.*— $\frac{1}{2}$  to 3 minims (0.03 to 0.18 ml.).

A white crystalline mass with characteristic anise odour and taste; m.p.  $22^\circ$  to  $23^\circ$ , congealing at  $21^\circ$  to  $22^\circ$ .

**Anthemis** (B.P.C.). *Syn.* ROMAN CHAMOMILE, FLOS CHAMOMILLÆ ROMANÆ (P. Helv. V).

The dried double or semi-double flowerheads of cultivated varieties of *Anthemis nobilis* (Compositæ). Tonic, aromatic and stomachic; emetic in large doses. The infusion ("chamomile tea," 1 in 20, *dose* 1 to 4 ounces) is a domestic remedy for indigestion, and a tincture (2 of fresh flowers in alcohol 90% 3 and water 1, *dose* 3 to 10 minims), has been given for summer diarrhœa of children. A decoction with poppy heads is used as a fomentation.

**Extractum Anthemidis** (B.P.C.) *Dose*—2 to 8 grains (0.12 to 0.5 g.)

The soft aqueous extract with added oil of chamomile

**Extractum Anthemidis Liquidum** (B.P.C.) *Dose*— $\frac{1}{2}$  to 1 drachm (2 to 4 ml.) 1 in 1

**Kamillosan** (Homburg Pharma Ltd, London). A pharmacologically tested and clinically effective preparation of fresh chamomile. Has disinfecting, deodorising and astringent properties. For enemas, fomentations and gargles.

**Oleum Anthemidis** (B.P.C.). *Dose.*— $\frac{1}{2}$  to 3 minims (0.03 to 0.2 ml.).

Distilled from anthemis. A blue liquid when freshly distilled (due to the presence of azulene) becoming greenish and then brownish-yellow. **Soluble** in less than its own vol. of 90% alcohol.

**Matricaria** (B.P.C.) *Syn.* GERMAN CHAMOMILE FLOWERS, FLOS CHAMOMILLÆ (P. Helv. V, P. Dan.).

*Dose.*—2 to 4 drachms (8 to 16 g.).

The dried flowerheads of *Matricaria Chamomilla*. They have a hollow conical receptacle and no paleæ, while the receptacles of *Anthemis nobilis* are solid and covered with concave, blunt, narrow bracts. Used for the same purposes as anthemis. Oil of German chamomile is inferior in odour to oil of *Anthemis nobilis*.

**Fœniculum** (B.P., P. Helv. V, P. Dan.).

*Syn.* FENNEL FRUIT.

*Dose.*—5 to 10 grains (0.3 to 0.6 g.)

The dried ripe fruits of cultivated plants of *Fœniculum vulgare* (Umbelliferae). Contains volatile oil.

Given to infants in form of Aqua Fœniculi.

**Aqua Fœniculi Concentrata** (B.P.C.)

*Dose.*—5 to 15 minims (0.3 to 1 ml.)

Contains 2% of oil and is approximately 40 times the strength of the distilled water.

**Aqua Fœniculi Destillata** (B.P.C.) *Dose.*— $\frac{1}{2}$  to 1 ounce (15 to 30 ml.). Represents 10% of fennel.

**Oleum Fœniculi** (B.P.C., U.S.P. XI).

*Dose.*— $\frac{1}{2}$  to 3 minims (0.03 to 0.2 ml.).

Contains anethole, also fenchone,  $C_{10}H_{16}O$ . **Soluble** 1 in 3 to 5 parts of alcohol 90%. Aromatic carminative, usually given as Aqua Fœniculi.

## ANTIMONIUM

Sb = 121.76.

[P1] "*Antimony, chlorides of, oxides of antimony, sulphides of antimony; antimonates, antimonites, organic compounds of antimony.*"

[81] "*Antimonial poisons except substances containing less than the equivalent of one per cent. of antimony trioxide*"

[86] "*Antimonial poisons—specify proportion as the proportion of antimony trioxide ( $Sb_2O_3$ ) or antimony pentoxide ( $Sb_2O_5$ ) that the preparation would be calculated to contain on the assumption that the antimony (Sb) in the poison had been wholly converted into antimony trioxide or antimony pentoxide as the case may be.*"

**Antidotes to Antimony Salts.**—Give emetic if vomiting has not occurred and wash out stomach with 180 gr. of tannic acid in 2 gallons of water, using stomach tube. Give 20 gr. of tannic acid in water and repeat 5 gr. doses every  $\frac{1}{2}$  hour for 4 or 5 doses. Keep patient warm and give demulcent drinks. Strychnine,  $\frac{1}{4}$  gr., hypodermically. Saline infusion may be necessary. Morphine,  $\frac{1}{4}$  gr., hypodermically, in cases of extreme irritability.

[P1 81] **Antimonii Arsenas.**

Dose— $\frac{1}{100}$  to  $\frac{1}{50}$  grain (0.0006 to 0.002 g.) twice or thrice daily. Max. single dose— $\frac{1}{10}$  grain (0.002 g.),  $\frac{1}{5}$  grain (0.02 g.) in 24 hours.

A mixture of antimonious oxide and 20% arsenic acid, a heavy white powder Used in syphilis and skin eruptions. Nerve and muscular tonic.

[P1 81] **Antimonii Oxidum (B P C)** ANTIMONIOUS OXIDE

$Sb_2O_3$  = 291.5

Dose—1 to 2 grains (0.06 to 0.12 g.)

A white powder, soluble in hydrochloric acid and in alkaline tartrate solution, caustic alkalis, etc. Diaphoretic, expectorant and emetic.

[P1] **Injectio Antimonii Oxidi.**

Dose.—15 to 30 minims (1 to 2 ml.), *subcutaneously, intramuscularly, or intravenously, increased as required.—Vide postea.*

These doses contain  $\frac{1}{100}$  and  $\frac{1}{50}$  gr. respectively in a solvent of equal parts of glycerin and water. Note.—20 ml. contains  $\frac{1}{2}$  gr. of antimony oxide =  $\frac{1}{2}$  gr. nearly of potassium antimonyl tartrate.

The antimony oxide, in fine powder, is heated with the glycerin, taking care to prevent the decomposition of the solvent, the water being added to the glycerin solution (warm). This produces a permanent preparation.

**Uses.**—Even with the small doses indicated the injection has been effective in American leishmaniasis, kala-azar, oriental sore and trypanosomiasis; stronger doses could, no doubt, be used in bilharziasis. The preparation in dose equal to even  $\frac{1}{50}$  gr. of tartar emetic is active, hence it is useful when treatment has to be extended over long periods.

In American leishmaniasis it may be given by subcutaneous, intramuscular or intravenous injection, the last-mentioned being



the most rapid *From 1 to 2 ml on alternate days or from 5 to 6 ml. of the solution weekly* Injections on alternate days appear to have more lasting effect.

[P1 81] **Pulvis Antimonialis** (B P C.). *Syn.* JAMES'S POWDER.

*Dose.*—3 to 6 grains (0.2 to 0.4 g.).

Contains 33½% of antimonious oxide in calcium phosphate

[P1 81] **Pilula Antimonii Conii et Quininae.**

*Dose.*—As required in fever

Antimonial powder 1 gr., extract of conium 2 gr., quinine sulphate 2 gr.  
Successful in a variety of febrile conditions, including malarial fevers

[P1 81] **Liquor Antimonii Chloridi** (B P C.) *Syn.* BUIFER OF ANTIMONY

A solution of antimonious chloride containing 17 to 18% w/w of Sb. Formerly used as an escharotic, now used mainly in veterinary practice and in furniture polishes.

[P1 81] **Antimonii et Potassii Tartras** (B P, U S P XI, F.E VIII, P. Belg IV, P. Helv V, P. Dan., and P. Ital V) *Syn.* POTASSIUM ANTIMONYL TARTRATE, TARTAR EMETIC, ANTIMONIUM TARTARATUM, TARTARALED ANTIMONY, ANTIMONY AND POTASSIUM TARTRATE, EMÉTIQUE (Fr. Cx.).

$C_4H_4O_7SbK, \frac{1}{2}H_2O = 333.9$

*Dose.*—Diaphoretic and expectorant  $\frac{1}{2}$  to  $\frac{1}{8}$  grain (0.002 to 0.008 g.), emetic  $\frac{1}{2}$  to 1 grain (0.03 to 0.06 g.) *Intravenously*  $\frac{1}{2}$  to 2 grains (0.03 to 0.12 g.), usually in 1 or 2% solution. *Hypodermically* it is painful, irritating and *not advised*, and *intramuscularly* it is too painful

*Fr. Cx.* has max. single dose 3 grains, max. in 24 hours 9 grains  
*P. Helv. V* max. in 24 hours 4½ grains

A single dose over limit of safety, i.e., between 0.01 and 0.02 g. per kilo weight, is sufficient to cause death—*Per J. trop. Med. (Hyg.)*, 1922, 300

*Alarming results may follow potassium antimonyl tartrate intravenously, due apparently to individual susceptibility or anaphylaxis—J. B. Christopherson and S. R. Gloyne, Lancet*, 1/1926, 227, 242

Asphyxia in a woman following 1 grain in 6% solution intravenously. Recovery after intracardiac injection of 0.2 ml. of 1 in 1000 adrenaline—*Lancet*, 11/1931, 1325.

Made by combining antimonious oxide with potassium acid tartrate. It occurs in colourless crystals or as a white powder.

**Soluble** 1 in 17 of cold water, 1 in 3 of boiling water and 1 in 20 of glycerin. Almost insoluble in alcohol 90% **Incompatible** with acids and alkalis, soap, and tannin

**Uses.**—Diaphoretic and emetic when given orally

In chorea in children it is less dangerous as emetic than apomorphine. It is an active remedy in acute bronchitis, often given in combination with opium. It is mainly used for the intravenous administration of antimony in the treatment of cutaneous leishmaniasis, frambæsia, filariasis, bilharziasis, espundia, kala-azar and oriental sore. Is also beneficial in relapsing fever and has been given with benefit in cerebrospinal fever. Is almost specific in granuloma inguinale.

For bilharziasis and kala-azar it is commonly given as a 2% solution in initial doses of  $\frac{1}{2}$  gr, increasing at each injection by  $\frac{1}{2}$  gr to a maximum of 2 gr. The injections are given on alternate days or twice weekly until 25 to 30 gr has been given. In filariasis more may be required (35 to 40 gr). During the course of the injections, red blood first disappears from the urine although smokiness remains until about 20 gr has been given. Injections should only be given with great caution if there is any lesion of the heart, lungs, kidneys or liver.

ACNE ROSACEA cured in 5 weeks by tartarated antimony,  $\frac{1}{2}$  gr *per os* thrice daily after meals, combined with application night and morning of a lotion containing sulphur, zinc oxide and magnesium carbonate. Good results also in furunculosis and ulcerative legs.—L. W. Bain, *Brit med J*, ii/1929, 51.

BILHARZIA "Rheumatic pains" liable to occur during the night following the 4th or 5th injection. There is increased hæmaturia as treatment proceeds, later, the blood and the ova vanish. Where there is intolerance, give brandy,  $\frac{1}{2}$  ml adrenaline solution and  $\frac{1}{2}$  ml post-pituitary extract intramuscularly. 10,000,000 infected Chinese on the Yangtse, and 6,000,000 people in Egypt.—J. B. Christopherson, *Lancet*, i, 1924, 1071. See also *Indian med Gaz*, Mar, 1925, 108.

In bilharzia its use is generally accompanied by cough, vomiting, and fainting.—M. Khalil and M. H. Betache, *Lancet*, i/1930, 234.

Exceeding the maximum dose causes sudden displacement of the bilharzia parasites, which lose their hold on the vein-walls and are precipitated as thrombi into the liver, possibly resulting in hepatitis, congestion of the bile ducts, or even septic foci in the pulmonary circulation, if not completely destroyed. The method of choice is gradual destruction over a period of one month.—F. G. Cawston, *J trop Med (Hyg)*, Feb 16, 1931.

**Rectal use** for bilharziasis: First dose 1 gr, then 2 gr every second day increasing to 3, 4 and 5 gr during 3 weeks in 100 ml of water. Less nausea and result, equal to intravenous injections.—H. F. Wilson, *Brit med J*, i/1922, 137.

A large single dose per rectum is the only rational treatment. As much as 19 gr have been given (not for bilharzia). After 6 gr in 4 oz of warm water, ova disappeared in a case. Half an hour in the recumbent position afterwards is enough. J. B. Anderson, *Brit med J*, ii 1925, 700.

CHANCROID well treated. 5 ml of a 1% solution intravenously, every second day or at longer intervals, 4 to 6 injections increased by 1 ml to a total of 12 ml.—H. Goodman, *J Urology*, April, 1925, 489, per *Prescriber*, 1926, 75.

Chancroidal ulcers well treated by application of 0.5% solution.—E. Rupel, *J Amer med Ass*, i/1926, 545. Also by intravenous injection of a 1% solution, initial dose 3 ml, increased by 1 ml up to 10 ml, injections at 4-day intervals.—A. E. Jones, *J Amer med Ass*, i/1927, 1699.

KALA-AZAR (compulsory treatment in Assam with tartar emetic intravenously "has converted a disease with a 90% mortality into one with a 90% rate of cure").—*Brit med J*, i/1925, 269.

KIRIAITIS well treated by tartar emetic intravenously.—F. G. Cawston, *J trop Med (Hyg)*, 1922, 127.

TRICHINOSIS (one case) well treated with tartar emetic, 3 to 4 ml of a fresh 2% solution intravenously for every 10 lb. weight. Injections given every second or third day, and dose gradually increased but not beyond 10 ml for every 10 lb weight.—J. S. Grove, *J Amer med Ass*, ii/1925, 350.

TUBERCULOUS DISLASE of the lungs and of the eye treated. Tartar emetic (intravenously) deserves further trial.—F. G. Cawston, *Brit med. J.*, i/1926, 820.

TUBERCULOUS HÆMOPTYSIS arrested with tartar emetic by the mouth—a total daily dose of 0.05 to 0.15 g, usually for 5 days, in pills containing 0.02 to 0.05 g with 0.01 g of opium, with water an hour before or after meals.—*Pr. Méd*, Oct 14, 1925.

TRYPANOSOMIASIS IN CATILE. Of value in *T. congolense* or *T. vivax* infections—1 g intravenously every 5 days for 6 doses. Of no value in horses infected with *T. brucei*.—Wenyon, p. 462. Successful in saving the lives of thousands of animals.—Ll. E. W. Bevan, *Trans R Soc trop. Med. Hyg.*, Aug, 1928, 154.

After a single course of tartar emetic injections relapses to *T. vivax* infection are the exception, whereas relapses to *T. congolense* infection are the rule.—H. E. Hornby, *Trans R Soc trop Med Hyg*, Jan, 1929, 403, also J. N. Hall, *ibid*

Following the use of the injections (in Swaziland) abscess formation round the injected jugular vein is very common, the injections often being attempted by the farmers themselves who rely on distilled rather than boiled water for making the solution. To control any local reaction from unskilful injections of stock infected with nagana it is recommended that the powder be dissolved in a 1 or even 2% solution of phenol and a little glycerin added.—F. G. Cawston, *J. trop. Med. (Hyg)*, 1935, 306.

[P1] **Castellani's Injection of Antimony Potassium Tartrate** (*Intramuscular*).

*Form No 1*

*Dose*.— $\frac{1}{2}$  to 1 ml every other day in the gluteal regions

Potassium antimonyltartrate 8 gr., liquefied phenol 10 m., glycerin 3 dr., water to 1 oz

*Form No. 2* contains  $\frac{1}{2}$  gr of sodium bicarbonate in addition

Both these produce some pain a few hours after administration

[P1] **Mistura Antimonii et Potassii Iodidi** (*Castellani*).

*Dose*.—One ounce diluted with 3 or 4 times the quantity of water thrice daily, for adults,  $\frac{1}{2}$  doses for children of 8 to 14 and for European patients

Potassium antimonyltartrate 1 gr., potassium iodide 1 dr., sodium bicarbonate 15 gr., sodium salicylate 10 gr., glycerin 2 dr (or syrup 1 dr or sodium tartrate 10 gr.), water to 1 oz

[P1] **Hauftus Emeticus Purgans** (*Mid H*)

Potassium antimonyltartrate  $\frac{1}{2}$  gr., magnesium sulphate 60 gr., water to 1 oz for a dose

[P1] **Vinum Antimoniale** (*B.P.C., P. Ned V, I.A*)

*Dose*.—10 to 30 minims (0.6 to 2 ml), as emetic 2 to 4 drachms (8 to 15 ml).

Contains 1 in 250 of potassium antimonyltartrate in sherry-type wine

Pneumonia is well treated by repeated 2 $\frac{1}{2}$  minim doses of antimonial wine. Crisis comes at the end of the fourth day

HEADACHE DUE TO HIGH BLOOD PRESSURE. Especially of value where chronic interstitial nephritis is a contraindication to blue pill.—A. Feilng, *Brit med J*, 11/1930, 907

[P1] **Mistura Vini Antimonialis** (*St J H*)

Magnesium sulphate 20 gr., antimonial wine 10 m., water to  $\frac{1}{2}$  oz

Will give very gratifying results in the early stages of many inflammatory diseases such as psoriasis or lichen planus.—J. E. M. Wigley, *Practitioner*, 1935, 359.

[P1 S1] **Unguentum Tartari Stibiati** (*P. Ital. V*)

Potassium antimonyltartrate 20 g., lanolin or soft paraffin 80 g

[P1] **Sterules of Antimony Potassium Tartrate** (*Martindale, London*) contain  $\frac{1}{2}$  gr. or 2 gr of potassium antimonyltartrate as 2% solution.

[P1 S1] **Antimonii et Sodii Tartras** (*B.P.*) Sodium Antimonyltartrate.  $C_4H_4O_7SbNa$  -- 308.8.

*Dose*.—As for Antimonii et Potassii Tartras

CAUTION.—One-third of the amount of antimony injected is excreted by the kidneys in 24 hours. Great caution required where heart, kidney or lung disease exists. In weak, emaciated and anæmic subjects begin with small dose gradually increased.—R. N. Chopra, *per J. trop. Med. (Hyg.)*, 1923, 133.

In colourless, hygroscopic scales or powder with sweetish taste.

**Manufacture**.—Boil antimonious oxide 10 in a solution of sodium acid tartrate 13 until almost clear (the quantity of antimonious oxide is purposely in slight excess). Filter and evaporate to dryness.

**Soluble** 1 in  $1\frac{1}{2}$  of water; insoluble in alcohol

**Uses.** This compound has properties similar to those of tartar emetic. Its greater solubility may be of some advantage and it is considered to be less irritant and less toxic than the potassium compound. It has been largely employed in bilharzia infection and in oriental sore and kala-azar in the same dosage as potassium antimonyltartrate

It has also been used in syphilis and in trypanosomiasis

GRANULOMA PUDENDI well treated Salvarsan useless—D J Maxwell, *J trop Med (Hyg)*, July, 1923, 235

KALA-AZAR well treated intravenously Begin with small dose, 0.5 ml of 2%, increasing by 0.5 ml up to a maximum of 5 ml, and continue for 2 to 4 months as required Heart, kidneys and lungs must function well—R N Chopra and L E Napier, *Indian med Gaz*, Jan., 1923

SYPHILIS treated intravenously Initial dose  $\frac{1}{2}$  gr increased to  $1\frac{1}{2}$  or 2 gr in 3 ml of water Results not inferior to those with arsenic—F G Cawston, *Brit med J*, 1/1922, 266

[P1] Sterules of Antimony Sodium Tartrate (Martindale, London) contain  $\frac{1}{2}$  gr or 1 gr in 2% solution

[P1 81] Antimonium Sulphuratum (B P C)

Dose—1 to 2 grains (0.06 to 0.12 g)

A mixture of the sulphides and oxides in orange red powder

**Uses.** Diaphoretic In syphilis and skin affections

[P1 81] Kermes Minerale (P Belg IV) is made by boiling black antimony sulphide (trisulphide) with sodium carbonate solution, and allowing the liquor to cool [P1 81] Tablettæ Kermetis (P Belg IV) contain 0.01 g

Dose—1 to 2 grains **Incompatible** with sodium bicarbonate and potassium acid tartrate

[P1 81] Antimonii Pentasulphidum (Fr. Cx, P Ned V, P Belg. IV, P Ital V, P Helv V, P Dan)  $Sb_2S_5 = 403.82$

An orange powder made by decomposing Schlippe's salt (sodium sulph-antimonate,  $Na_3SbS_5 \cdot 9H_2O$ ) with dilute sulphuric acid

[P1 81] Antimonium Nigrum Purificatum (P Belg IV, P Helv V)  $Sb_2S_5 = 339.7$

Greyish crystalline powder obtained by purification of native antimony sulphide Decomposed by boiling hydrochloric acid Used in veterinary practice as parasiticide

[P1 81] Stibium Sulfuratum (Trisulfuro) Crudum. Syn. STIBINA OR ANTIMONIO CRUDO (P Ital V) is converted into [P1 81] Stibium Sulfuratum depuratum, syn STIBINA DEPURATA, by treatment with ammonia FE VIII is similar

[P1 81] Antimony Crocus—For veterinary use, is a mixture of trioxide (about 4 parts) and trisulphide (1 part) Formed by heating equal weights of antimony trisulphide and potassium nitrate to which  $\frac{1}{2}$  of hydrochloric acid has been added—U S D

**Colloidal Antimony** has been given intramuscularly in leprosy, leishmaniasis, and pulmonary tuberculosis.

PULMONARY TUBERCULOSIS—0.5 ml. intramuscularly into the flexor muscles of the arm twice weekly, of value; the treatment can be carried out in the outpatient clinic without fear of untoward reactions No ill-effects from some thousands of injections Injections might be continued until physical signs have cleared up—P Moxey, *Brit med J*, 1/1927, 374.

"CREEPING ERUPTION" successfully treated with intramuscular colloidal antimony or intravenous tartar emetic injections—F G Cawston, *Brit. med. J*, 11/1928, 207.

### Organic Antimony Compounds.

The organic antimony compounds used in the treatment of leishmaniasis may be classed as:

(1) Salts of *p*-aminophenylstibinic acid, among which are included Stibamine and Neostibosan;

(2) Derivatives obtained by substitutions in the amino group of *p*-aminophenylstibinic acid, including Stibenyl and Neostam;

(3) Derivatives obtained by substitutions in the benzene nucleus of *p*-aminophenylstibinic or *p*-acetylaminophenyl stibinic acid

[P1 81] **Anthiomaline** (*Pharmaceutical Specialities (May & Baker) Ltd., London*) Lithium antimony-thiomalate. An organic compound containing 16% of antimony. *Dose*—From 0.5 to 2 ml (1 ml = 0.01 g Sb) intramuscularly, for a course of 12 to 20 injections, at the rate of 2 or 3 a week. In lympho-granuloma inguinale, bilharziasis and leishmaniasis. Has low toxicity and is well tolerated.

**BILHARZIA**—2 ml of Anthiomaline is a sufficiently large repeated dose for a child, and 4-ml doses should not be exceeded in adults. Excessive doses cause salivation or retching. A cure may sometimes be obtained in less than the month usually required with tartar emetic.—F. G. Cawston, *Prescriber*, 1936, 233.

[P1 81] **Antimosan** (*Heyden, Dresden, Braun, London*) A 5% solution of "Heyden 661" which contains 12.5% of trivalent antimony. For intramuscular or intravenous use. Initial dose 2 ml increasing to 6 to 8 ml. Has trypanocidal action and is advocated in multiple sclerosis.

[P1 81] **Fouadin** (*Bayer Products, London*) Sodium antimony pyrocatechindisulphonate in 6.3% isotonic solution. *Dose*—Initial dose intramuscularly 1.5 ml increasing to 5 ml with injections every second day and total dosage of about 50 ml.

**BILHARZIA**—Because of its inferior antimony content Fouadin cannot be recommended in the treatment of bilharzia except where intravenous injections are impossible and where treatment can be repeated if found necessary.—F. G. Cawston, *J. trop. Med. (Hyg.)*, 1936, 29.

**DISSEMINATED SCLEROSIS**—A course of 10 or 12 intramuscular injections of Fouadin is often very helpful.—Macdonald Critchley, *Med. Pr.*, 1/1936, 520.

**GRANULOMA INGUINALE**—Fouadin a safe and rapid specific. Generally superior to potassium antimonytartrate and without dangerous reactions.—*Amer. med. Ass.*, 1/1933, 1674.

**SCHISTOSOMIASIS** cured by intramuscular injections of 1 to 5 ml of 7% solution. Local reaction slight, and no deaths or serious symptoms occurred in 20 cases. 2 weeks treatment gives cure.—*Brit. med. J. Epit.*, 11/1929, 92.

**Schistosomiasis in W. African children**. Given intramuscularly, the total course of treatment being equivalent in ml to the weight of the child in kilos, given in 10 doses, the third to the tenth being equal and given on alternate days, the first injections given on consecutive days and being about 30% and 70% respectively of succeeding full doses. Of 6 cases treated all were clear of ova by the twenty-fourth day, but there was loss of weight and considerable local pain.—R. M. Gordon and E. P. Hicks, *Ann. trop. Med. Parasit.*, Oct 22, 1930.

Nine intramuscular injections for an adult cure in the majority of cases. First day, 1.5 ml, second, 3.5 ml, third, 5 ml, fifth, 5 ml, seventh, 5 ml, ninth, 5 ml, eleventh, 5 ml, thirteenth, 5 ml, fifteenth, 5 ml. If ova found give further two doses.—M. Khalil and M. H. Betache, *Lancet*, 1/1930, 234.

Advantages over tartar emetic—duration of treatment 10 days less, and absence of local complications. Disadvantages—greater expense, sometimes causes bradycardia, preparation a monopoly.—*Brit. med. J.*, 11/1931, 1191.

**UNDULANT FEVER**—Eight cases at Malta successfully treated by intramuscular injection of 1.5 ml. on the first day, 3.5 ml. on the second day, followed by 5 ml. on alternate days. As a result of the injections, there were no waves of fever after the first, though such waves are one of the characteristics of the disease.—C. Z. Neumann, *Lancet*, 1/1936, 1001.

[P1 81] **Neostam** (*Burroughs Wellcome, London*) A brand of stibamine glucoside (the nitrogen-glucoside of sodium *p*-aminophenylstibonate) available in phials of 0.05, 0.1, 0.2, 0.5, 1 and up to 5 g for use in kala-azar, etc. *Dose*.—0.1 g per 100 lb. body weight intravenously as a 4% solution in distilled water on alternate days until 3 g per 100 lb *b/w* has been given.

[P1 81] **Neostibosan** (*Bayer Products, London*). *Syn.* "693 B." Diethylamine-*p*-aminophenyl stibinate. Now supersedes both Stibenyl and Stibosan. In kala-azar. *Initial dose*.—0.05 to 0.2 g according to age intravenously, 8 injections on 8 consecutive days for intensive treatment. *See also Brit. med. J. Epit.*, 1/1931, 65.

**MEDITERRANEAN VISCERAL LEISHMANIASIS**. The pentavalent preparations have attained their maximum effect and most convenient form in Neostibosan. With tartar emetic and Neostibosan almost 100% of cures have been obtained during the last few years. Contraindications are profound renal lesions and serious cardiac disorders.—Caronia (Italy). Neostibosan has yielded excellent results.—Sergent (Algiers). Results with Neostibosan highly favourable.—70% of cures.—Pittaluga (Spain).—*Quart. Bull. Hlth Org. L.O.N.*, Dec., 1935, 801.

[P1 81] **Stibenyl** (*Heyden, Dresden, Braun, London*). *p*-Acetylamino-phenylstibinate of sodium containing 33% of organically combined antimony. *Dose*.—0.1 g gradually increasing to 0.4 g, intravenously or intramuscularly in aqueous or physiological saline solution. In leishmaniasis, kala-azar, bilharziasis, etc.

[P1 81] **Stibosan** (*Heyden, Dresden, Braun, London*). *m*-Chlor-*p*-acetylamino-phenylstibinate of sodium, containing 31% antimony. *Dose*.—0.2 to 0.3 g as a 1 to 2% solution, intramuscularly or intravenously.

[P1 81] **Urea Stibamine** is composed of urea and *p*-aminophenylstibinic acid,  $\text{NH}_2\text{C}_6\text{H}_4\text{SbO}(\text{OH})_2$ , but apparently not a definite compound.

Safer than tartar emetic. An effective intravenous dose stated to be 0.25 g.—U. N. Brahmachari, *Ind. J. med. Res.*, 1922, *Yearb. Pharm.*, 1923, 64. *See also J. trop. Med. (Hyg.)*, 1924, 203, *Ind. med. Gaz.*, 1924, 391, 464.

**KALA-AZAR**. Intravenous injections on alternate days, starting with 0.1 g in cold sterile water, increasing by 0.05 g to a maximum of 0.25 g and continued for subsequent doses. Rapidity of disappearance of symptoms compared with sodium antimonyl tartrate, 2 to 3 weeks as against 3 months.—H. E. Shortt and Ram Taran Sen, *Indian med. Gaz.*, 1923, 289.

Reactions following administration.—L. E. Napier, *ibid.*, Nov., 1926, 559.

*See also* N. Chatterjee, *ibid.*, June, 1926, 284, 291.

Further notes on kala-azar treated with organic antimony compounds.—U. Brahmachari and co-workers, *Trans. R. Soc. trop. Med. Hyg.*, Apr., 1930, 617. Nov. 25, 1930, 351.

It was found at the Peiping Union Medical College that an adequate course of urea-stibamine (in kala-azar) for a child was 1.0 to 1.5 g, as contrasted with 1.5 to 2.5 g for Neostibosan. For an adult the figures were 1.5 to 2.5 g and 4.0 to 5.0 g. Urea-stibamine is thus definitely more potent than Neostibosan which, on the other hand, has the advantage of being a definite chemical compound of a lower toxicity. After treatment with either of these drugs patients must be followed for at least 7 months to a year before cure can be pronounced.

—C. U. Lee and C. I. Chu, *Chinese med. J.*, 1935, 328.

## APIOL

### B P C, P Belg IV

*Dose*.—3 to 10 minims (0.2 to 0.6 ml), in perles 3 minims in each, or capsules 3, 5 and 10 minims in each.

Apiol is obtained by alcoholic extraction from the fruit of *Carum Petroselinum*, *syn.* *Apium Petroselinum*, *Petroselinum sativum*, common parsley. The alcohol is evaporated and the residue allowed to cool, the clear liquid being decanted. It is a green oil, with a peculiar odour and a pungent taste like parsley. Sp. gr. 1.055 to 1.091.

**Soluble** readily in alcohol and ether.

The only substance to which the name apiol can be correctly applied is the crystalline stearoptene, previously in the *Fr. Ch.*. The essential oil of parsley appears to be the only body worthy of the name liquid apiol, and that only from an apiol-bearing variety of parsley.—J. F. Walmsley, *Pharm. J.*, 11/1928, 89.

Apiol has decided efficacy in primary amenorrhœa or deficiency of secretion, as well as in dysmenorrhœa. Should be given night and morning for 4 or 5 days during the period.

**Toxic Effects.** Clinical observations on 37 women with toxic polyneuritis following the use of apiol as an abortifacient.—R. Carrillo and J. W. G. T. Braak, per *J. Amer. med. Ass.*, 11/1932, 698.

Polyneuritis frequently follows its administration. Due to tri-ortho-cresyl phosphoric acid of which apiol contains 28 to 50% —*Brit med J. Epit.*, 1/1933, 12.

Three cases of polyneuritis following use of apiol as an abortifacient, due to the presence in it of tri-ortho-cresyl phosphate.—J. J. Waite, per *Brit. med. J. Epit.*, 11/1933, 5.

**TRI-ORTHO-CRESYL PHOSPHATE** The use of this compound (which is normally used in the manufacture of imitation leather) in the preparation of a synthetic ginger extract, caused an epidemic of peripheral motor paralysis of the legs and arms 20,000 cases of paralysis due to the drinking of this imitation ginger extract occurred in the South-East of the United States in 1930 before the cause was discovered. Very few deaths resulted, but partial recovery occurred only after some months, and in many cases the paralysis seems permanent. The economic loss was estimated at more than £10,000,000. This paralysis is only produced by tri-ortho-cresyl phosphate it is not produced by ortho-cresyl, or by para- or meta-tri-cresyl phosphate —*Brit med J.*, 11/1933, 579

#### [P1 81] Capsules of Liquid Apiol and Ergotin.

Contain apiol 5 minims (0.3 ml.) and extract of ergot 2 grains (0.12 g.).

[P1 81] **Ergoapiol** (*Martin H. Smith, New York, Christy, London*). Capsules containing the active principles of ergot and apiol are supplied for amenorrhœa, dysmenorrhœa and allied disorders.

#### **Oleum Petroselinii** (*B.P.C.*) *Syn.* OIL OF PARSLEY.

*Dose* —3 to 5 minims (0.2 to 0.3 ml.)

The oil distilled from the fruit of parsley, *Carum Petroselinum*. A viscous colourless or yellowish oil, resembling apiol in properties.

**"Green Apiol"** is obtained by extracting the fruits with ether and evaporating the solvent. It has a lower sp. gr. than apiol (about 0.93). This may be purified to yield a viscous, oily, yellow, liquid apiol.

**Apiolum** (*F.E. VIII*). *Syn.* APIOLE, CRYSTALLINE APIOL, "WHITE APIOL," ÉTHER MÉTHYLÉNIQUE ET DIMÉTHYLIQUE DE L'ALLYL-APIONAL, CAMPHRE DE PERSIL

$\text{CH}_2\text{O}_2\text{C}_6\text{H}(\text{OCH}_2)_2\text{CH}_2\text{CH}\cdot\text{CH}_2 = 222.1$ .

In acicular crystals, slightly soluble in water, readily soluble in chloroform, ether and alcohol 90%. M.p. 29° to 30°.

For amenorrhœa a solution in olive oil containing 3 grains (0.2 g.) in 15 minims (1 ml.) has been given—injecting once daily for some days before the period. Also given as a quinine substitute in malaria.

**Dill-Apiole**,  $\text{C}_{12}\text{H}_{14}\text{O}_4$ , is an isomeric substance obtained from oil of Indian dill (*Anethum Sowa*).

**Apium** (*B.P.C.*). *Syn.* CELERY FRUIT, CELERY SEED.

*Dose*.—20 to 60 grains (1.2 to 4 g.).

The dried ripe fruits of cultivated plants of celery, *Apium graveolens* (*Umbelliferae*). Contain 2 to 3% of volatile oil. Nervine sedative and tonic. The decoction (1 in 20) is a domestic remedy

for rheumatism The entire herb is used in "Sirop des Cinq Racines."

**Extractum Apii Liquidum** (B.P.C.) Dose—5 to 20 minims (0.3 to 1.2 ml.). 1 in 1

**Oil of Celery.** Dose— $\frac{1}{2}$  to 3 minims or more. Capsules are made  $3\frac{1}{2}$  and 5 minims. Contains a small proportion of apiol. Antispasmodic and nerve stimulant

In rheumatoid arthritis 5 to 15 minim doses have been used successfully. It acts probably as an intestinal antiseptic

## APOMORPHINÆ HYDROCHLORIDUM

B.P., U.S.P. XI, P. Helv. V, P. Jap., P.G. VI, P. Ned. V  
 $C_{17}H_{17}O_2N, HCl, \frac{1}{2}H_2O = 312.6$ .

Syn. CHLORETUM APOMORPHICUM (P. Dan., P. Ital. V, F.E. VIII, P. Belg. IV).

[P1] "*Alkaloids, the following; their salts, simple or complex.—Apomorphine*"

[81] "*Alkaloids, the following; their salts, simple or complex.—Apomorphine except substances containing less than 0.2% of apomorphine.*"

Dose— $\frac{1}{64}$  to  $\frac{1}{16}$  grain (0.001 to 0.002 g.), increased, as an expectorant;  $\frac{1}{32}$  to  $\frac{1}{8}$  grain (0.002 to 0.008 g.) hypodermically as an emetic and hypnotic. The oral dose as an emetic is  $\frac{1}{16}$  to  $\frac{1}{4}$  gr (0.006 to 0.016 g.)

A derivative of morphine or codeine obtained by heating them with an excess of hydrochloric acid in sealed tubes. In commerce the hydrochloride occurs in greyish white, acicular crystals which become greenish on exposure to air and light.

**Soluble** 1 in 60 of water, 1 in 5 of alcohol 90%. Almost insoluble in ether and chloroform. A trace of acid prevents solutions turning green, *vide* *Injectio postea*

**Incompatible** with sodium carbonate and bicarbonate, tannin and iron salts

**Antidotes.** Give repeated  $\frac{1}{2}$ -dr doses of aromatic spirit of ammonia in water, or ammonia inhalations. Keep patient lying down and warm

**Uses**—In all cases of non-corrosive poisoning it is of great value as an emetic. It is an anti-stimulant, in bronchial asthma doses of  $\frac{1}{8}$  grain are very useful. Small doses are expectorant and relieve bronchitis and pertussis. In puerperal convulsions it soon causes vomiting and free perspiration, patient sleeps and awakes quiet

In a case of obstruction of the oesophagus by a plum-stone, the injection of apomorphine hypodermically caused its removal

[P1 81] **Injectio Apomorphinæ.**

Apomorphine hydrochloride 1, dilute hydrochloric acid 1, distilled water to 100  $\frac{1}{16}$  gr. in 11 m

Dose.—5 to 10 minims (or more) as an emetic. The addition of the trace of acid keeps it stable and colourless.



The effect produced by a small injection on a mad-drunk patient is remarkable. As hypnotic  $\frac{1}{15}$  to  $\frac{1}{10}$  grain. The patient, however wild, sleeps 12 hours and awakes refreshed.

[D P1 81] **Mistura Apomorphinæ Composita.** *Syn.* MISTURA TUSSIS, *Luff*  
*Dose* —  $\frac{1}{2}$  ounce every 4 hours.

Apomorphine hydrochloride  $\frac{1}{8}$  gr, morphine hydrochloride  $\frac{1}{4}$  gr, diamorphine hydrochloride  $\frac{1}{4}$  gr, dilute hydrochloric acid 5 m, syrup of wild cherry  $\frac{1}{2}$  dr, chloroform water to  $\frac{1}{2}$  oz.

A palatable mixture useful for irritable cough, especially post-influenzal cough. The hydrochloric acid effectually prevents the precipitation of any of the alkaloids.

[P1] **Syrupus Apomorphinæ (B.P.C.).**

*Dose.* —  $\frac{1}{2}$  to 1 drachm (2 to 4 ml.).

Contains  $\frac{3}{16}$  gr. of apomorphine hydrochloride in 1 dr

## AQUÆ

The aromatic waters of the *B P* and *B P C* are of the following types.—

- (1) Distilled aromatic waters which are prepared by distilling the drug or volatile oil with water. *If the prescriber requires this type of water to be dispensed, it must be specified as "distilled" on the prescription.*
- (2) Waters prepared by one of the following methods —
  - (a) Shaking the essential oil with 500 times its volume of distilled water at intervals and filtering after 12 hours
  - (b) Triturating the oil with powdered talc, diatomite, calcium phosphate or pulped paper and 500 times its volume of distilled water, and finally filtering
  - (c) Diluting a concentrated water with 39 times its volume of distilled water and filtering if necessary through diatomite or other medium

### Aquæ Concentratæ.

These are now official in the *British Pharmacopœia*, and are prepared by dissolving the volatile oil in alcohol (90%) and then gradually adding distilled water, shaking after each addition. The cloudy preparation is then clarified by shaking with talc, which probably removes some of the terpene content of the volatile oil. The final alcoholic content of the preparations is between 52 and 56% v/v of ethyl alcohol, and consequently they will keep satisfactorily. These concentrated waters when diluted with 39 times their volume of distilled water yield preparations which are approximately equivalent in strength to the distilled waters, except that such dilutions will contain a little alcohol. The distilled aromatic waters are usually of finer aroma

## ARGENTUM

Ag = 107.88.

**Argenti Acetas.**  $\text{CH}_3\text{COOAg}$  = 166.9.

In white crystals, **soluble** in water. A 1% solution is useful

for purulent ophthalmia in infants Dilute salt solution may be used after it

OPHTHALMIA NEONATORUM is prevented by silver acetate as well as by the nitrate, causes less catarrh—*Brit med J Fpit*, 1/1926, 39

[P1 81] **Argenti Cyanidum.**  $\text{AgCN} = 133.9$

Dose —  $\frac{1}{64}$  to  $\frac{1}{8}$  grain (0.001 to 0.003 g.)

White powder containing 80.48% Ag. Antipyretic occasionally used in epilepsy and chorea

**Argenti Iodidum.**  $\text{AgI} = 234.8$

In the freshly precipitated form this salt has been used in cases of ophthalmia It has astringent properties Efficacious in gonorrhoeal ophthalmia One drop of weak solution instilled 3 times a day or oftener in cases of extensive chemosis and danger of corneal sloughing

Corneal opacities, conjunctivitis and pannus have been treated, commencing with 1% strength In ulcer of the cornea it should be used cautiously

A 5% silver iodide emulsion makes a good opaque medium for cystography, and has soothing antiseptic action on the bladder. Also of value for urethrograms

**Nascent silver iodide** in 3% suspension may be produced from silver nitrate 2.2 g., potassium iodide 2.2 g., distilled water 50 ml., mucilage of Irish moss to 100 ml. For a light flocculent precipitate dissolve each in 50 ml. of water. To produce a coarse precipitate the salts are separately dissolved in 5 ml. of water, shaken and diluted with the mucilage Gelatin 0.3% has also been used to dissolve the potassium iodide

**Neo-Protosil** (*Parke, Davis, London*) A colloidal silver iodide compound prepared with a soluble protein base Contains 20% of silver iodide Used in solution for treatment of inflammations of the mucous membranes of the eye, nose, throat, etc

**Argenti et Potassii Iodidum.**  $\text{KAgI}_2$  400.8 *Syn* SILVER POTASSIUM IODIDE

The double iodide of potassium and silver A crystalline substance readily soluble in water Silver iodide is precipitated on dilution but precipitation is not complete until a fairly high dilution is reached

**Preparation of an injection.** One part of crystallised silver potassium iodide and 4 parts of potassium iodide are dissolved in water, as required, in strengths of 0.5 g., 1 g. and 1.5 g., in 20 ml. in each case Each of the dilutions contains a fine suspension of silver iodide and a solution of the double salt

**GONORRHOEA** The injection of 20 ml. into the ineatus (apply tight bandage over glans for 15–30 minutes after injection), causes a rapid decrease of discharge after 6 injections and a complete disappearance of gonococci after 12 to 15 injections Injections need only be given twice or thrice weekly, as silver iodide persists in the urethra—S. R. Naidu, *Brit med J*, 1/1927, 139

**Argenti Nitras** (*B.P., U.S.P. XI, P. Helv. V, P. Dan.*)  $\text{AgNO}_3 = 169.9$  *Syn* LUNAR CAUSTIC

Dose —  $\frac{1}{8}$  to  $\frac{1}{4}$  grain (0.008 to 0.016 g.) in a pill, best with kaolin ointment as an excipient Up to  $\frac{1}{2}$  grain has been given *U.S.P. XI* average dose  $\frac{1}{8}$  grain.

**Incompatible** with organic material, e.g., rose water, if used instead of distilled water for preparing a lotion or pigment; also with tartaric acid, hydrocyanic acid, iodine and halides.

**Soluble** 1 in 0.53 of water and 1 in 25 of alcohol 90%; slightly soluble in ether and glycerin.

**Antidotes.** Empty stomach by stomach tube, using 2 oz. of sodium chloride in 2 gallons of water, or give  $\frac{1}{4}$  oz. sodium chloride in 1 pint of water or milk, followed by an emetic. Demulcent drinks. Castor oil. Morphine,  $\frac{1}{4}$  gr. hypodermically for pain, if necessary.

**Silver nitrate stains** on the skin may be removed with mercuric chloride solution, or with potassium cyanide solution, or by wetting the skin and rubbing potassium iodide on the stain, leaving it on for a few hours

In argyria a mixture of 1% of potassium ferricyanide and 6% of sodium thiosulphate injected intradermally removes a large part of the silver from the skin in old cases with deep pigmentation. A small dose of morphine and atropine cuts short sting of the injection —A. W. Stillians and T. K. Lawless, *J. Amer. med. Ass.*, 1/1929, 21.

Occupational argyria in silver nitrate workers and silversmiths —J. M. Harker and D. Hunter, *Brit. J. Dermat.*, 1935, 441.

**Uses.** As a caustic and stimulant to promote healing. Small doses internally check diarrhœa of children. In typhoid, where there is hæmorrhage  $\frac{1}{8}$  grain every 3, 4 or 6 hours, or even as often as every 2 hours. Rectal injections are also useful for the bleeding of dysentery (60 grains in 3 pints). In laryngeal phthisis a spray  $\frac{1}{4}$  to 2 gr. to the ounce

In vomiting of pregnancy  $\frac{1}{8}$  grain in a wine-glass of water every 6 hours has been found effective. In gastric ulcer  $\frac{1}{8}$  grain in a pill 3 or 4 times daily half an hour before food useful. Solutions have also been used. In eczema of the flexures and particularly of mucous surfaces, a 2 to 3% solution, alternating with Lotio Calaminæ Oleosa, is valuable. Pigments, 1 to 5%, are used for the throat in pharyngitis and laryngitis, and applied to ulcers as a stimulant. Lotions for pruritus ani or vulvæ and eye-drops vary from 1 in 1000 to 1 in 100. 1% eye drops are applied for the prophylaxis of ophthalmia neonatorum. Purulent ophthalmia and ulcerative blepharitis are treated with 1 to 2% drops. Ulcerative stomatitis is well treated by 0.5 to 2% solution.

Glycerin 15% added to  $\frac{1}{4}$  to 2% silver nitrate solution renders it less painful, and possibly more effective

**Urethral and Vaginal Injections.** 0.02 to 0.2% (1 in 5000 to 1 in 500) is usually employed

In lavage of the entire urethra in cystitis and for epithelial tumours of the urinary bladder 2 grains to the pint (1 in 5000 approx.) is sufficiently strong. In some cases it may be advisable to commence with a quarter of this strength. Hydrostatic pressure may be used, *i.e.*, the container being about 5 feet above the couch, instead of a syringe.

**Urethral Bougies** of silver nitrate contain  $\frac{1}{8}$  grain with theobroma basis. Give good results in obstinate cases of gonorrhœa

**BURNS.** Spray or paint a 1% silver nitrate solution on burn and expose for 1 to 5 minutes to mercury vapour or tungsten arc lamp at 6 to 20 inches distance, or to real sunlight for  $\frac{1}{4}$  hour. No dressings used. Repeat if necessary in 24 to 36 hours.—*Brit. med. J.*, ii/1929, 668.

**ERYSIPELAS** in the newborn treated with 4% solution, the lesion being swabbed 4-hourly day and night. The erysipelas tends to subside after 3 days' treatment, the average duration of which is 21 days. The treatment is almost painless—H. Graner, *see Med Annu*, 1935, 135

**Gutt. Argent Nitr.** (*N.I.F.*)

Silver nitrate 1 gr., distilled water to 2 dr. (approx 0.5%)

**Liquor Argenti Nitratis**, (*R.L.O.H.*). 4 to 8 gr to 1 oz of sterilised water (1 to 2 % approx).

As prophylactic, drops should not be used in stronger solution than 1%, and caution needed if used more than once or twice. Case of conjunctival hæmorrhage following 5 instillations of 1.5% solution—*Lancet*, 1/1928, 716

**Pigmentum Argenti Nitratis Æthereum** (*L.H.*)

Silver nitrate 10 gr., water 1 dr., spirit of nitrous ether to 1 oz

Caustic even when painted on a greasy skin. 3 to 10 grains to the ounce relieves pruritus ani and pruritus vulvæ. Useful in eczema and for prevention of bedsores

**[D P1 81] Pilula Argenti Nitratis et Morphine Acetatis.** *Syn* CROCC'S PILL. Contains ½ gr. of each salt, made with kaolin ointment

**Unguentum Argenti Nitratis Compositum.** *Syn* UNGUENTUM BILLROTHI (*P. Ned V*)

Silver nitrate 1, balsam of Peru 5, yellow soft paraffin 94

**Nargol Bougies** (*Parke, Davis, London*) Urethral bougies of silver nucleide 1% and 2%. Treatment of specific urethritis.

**Partagon Bougies** (*Sandoz, London, Brooks & Warburton, London*) Bougies of silver nitrate associated with selected organic colloids. Supplied for men in two strengths "mild" (0.75%  $\text{AgNO}_3$ ) and "strong" (2%  $\text{AgNO}_3$ ), and for women in one strength (1.5%  $\text{AgNO}_3$ ).

**Phllonin** (*Promonta, Hamburg, Pharmaceutical Products, London*) Ointment containing silver nitrate, copper iodo-ortho-quinoline sulphate, an acridine derivative, zinc oxide, Peru balsam, and irradiated cholesterol. For all types of skin infections

**Argenti Nitrates Induratus** (*B.P.*) *Syn.* TOUGHENED CAUSTIC. Contains 5% of potassium nitrate moulded into caustic points. *U.S.P. XI* has 94.5%  $\text{AgNO}_3$ .

**Argenti Nitrates Mitigatus** (*B.P.C., P. Helv. V*) *Syn.* MITIGATED CAUSTIC, ARGENTI NITRAS DILUTUS

Silver nitrate 1, potassium nitrate 2, fused together and moulded into sticks for use as caustic. *P. Jap.* uses equal parts

**Argenti Oxidum** (*B.P.C.*)  $\text{Ag}_2\text{O} = 231.8$

*Dose.*—½ to 2 grains (0.03 to 0.12 g.) in a pill with kaolin ointment.

Is not so caustic in action as silver nitrate. Continued administration may discolour the skin. It readily yields its oxygen, and will explode if mixed with such bodies as phenol and creosote.

**Soluble** very slightly in water, insoluble in alcohol 90%.

**Uses.** Has been given in epilepsy, chorea and dysentery. It stains the skin less than the nitrate

**Argentoproteinum** (*B.P. Add*). *Syn. and Prop. Names.* ARGENTI PROTEINAS (*B.P.C.*), ARGENTUM PROTEINICUM (*P.G. VI, P. Ital. V, P. Jap. IV, P. Ned. V, F.E. VIII, P. Belg. IV, P. Helv. V*), ARGENTUM PROTEINICUM FORTE (*U.S.P. XI*), STRONG SILVER PROTEIN, SILVER PROTEIN, ARGEIN (*Allen & Hanburys, London*), PROTARGOL (*Bayer Products, London*).

*Dose.*—1 to 3 grains (0.06 to 0.2 g.) No dose is given in *B.P. Add*

**Note.**—The *U.S.P.* *XI* names, Strong Silver Protein for preparations containing 8% of Ag and Mild Silver Protein for those containing 20% or more of Ag, are based on the fact that the former are the more strongly bactericidal. They are also more irritant.

A fine, brownish-yellow, somewhat hygroscopic powder containing 7.5 to 8.5% of Ag. *P. Svec.* has 7.8 to 10% of Ag.

**Soluble** about 1 in 2 of water, almost insoluble in alcohol, chloroform and ether. Aqueous solutions may be prepared by shaking on to surface of cold water and allowing to dissolve slowly, or by triturating to a cream with water and diluting as required.

**Preparation of Colloidal Silver and Silver Proteinate.** Add slowly with constant stirring 1 kg. of casein to a hot solution of 0.5 kg. sodium hydroxide solution (40° Bé, sp. gr. 1.383) and 2 l. of water. Dilute with half its volume of water, cool and filter. Acidify with nitric acid diluted with 2 parts of water and knead the precipitated protalbic acid with water to remove nitric acid, adding the washings to the mother-liquor which contains lysalbic acid. Dissolve the protalbic acid in warm water containing ammonium hydroxide, re-precipitate with nitric acid and repeat the solution and precipitation until a pearly, wax-like substance results. This is again dissolved in ammonia, the solution filtered and evaporated and the protalbic acid dried to constant weight at 105° (yield about 160-170 g.). Dry protalbic acid 19 g. in 15% solution is mixed thoroughly with silver oxide freshly precipitated from 100 g. of silver nitrate by means of sodium hydroxide, and washed free from nitric acid by decantation. Add to the mixture 18 g. of sodium hydroxide and 3 to 5 ml. of solution of ammonia (s.g. 0.910) and heat on a water-bath at 80° until a portion of the liquid diluted with water is faintly opalescent by reflected light, but clear by transmitted light. The solution is dialysed for two days and then dried in thin layers at 60° to 80°. Yield about 80 g.

**For Silver Proteinate.** The mother liquor and washings obtained as above are dialysed free from nitrates. The liquid is neutralised to phenolphthalein with sodium hydroxide, and the proportion of lysalbic acid determined by drying a portion of the solution at 105° and ashing the dry powder, the difference between the weights of ash and dry powder gives the lysalbic acid. Lysalbic acid 1 kg. is diluted with water to form an 8% solution to which is added a solution of 155 g. silver nitrate in 500 g. of water. The mixture is heated on a water-bath at 80° until clear, and is then diluted and dialysed for five days. The liquid is evaporated under reduced pressure to the consistence of a thick syrup, solution of hydrogen peroxide is added slowly with constant stirring until the desired light brown colour is obtained, and the product is dried below 60°, preferably under reduced pressure.—*R. A. Feldhoff, Apoth. Ztg.*, 1933, 83, 1205.

**Incompatibility with Alkaloids.** Solutions of many silver-protein compounds are alkaline and precipitate alkaloids from solutions of their salts. Where the combination of silver-protein compound and cocaine is necessary, cocaine nitrate should be prescribed.—*Pharm. J.*, 1/1932, 282.

**Uses.** Compounds included in this group are used as local antiseptics for similar purposes to silver nitrate, but have the advantage of being non-corrosive, non-astringent, and unaffected by body secretions. They are especially useful for application to the mucous membrane. For the urethra, 1 to 2% solutions are used, or in chronic gonorrhœa up to 10%. Pessaries and bougies for use in gonorrhœa are made with 5 to 10%. A 0.5% agar jelly containing 0.5% of silver protein (Schindler's jelly) has also been applied to the urethra in gonorrhœa.

For ophthalmic use  $\frac{1}{4}$  to 1% (or stronger up to 10%) and from 4 to 20% for wounds and ulcers. Stains the conjunctiva to some extent. Ointments 5 to 10%.

Solutions should be freshly prepared since old solutions may be slightly caustic.

**Guttæ Argenti Proteinatis (R L O H)**

Silver protein 8, 20, 40 or 60 gr, sterilised water to 1 oz

**Neissers Bougies.** Silver proteinate 1%, phenazone 2%, in oil of theobroma or in gelatin basis. For the treatment of gonorrhœa

**Hegonon (Schering, London)** Ammoniacal silver nitrate derivative of albumose containing 7% Ag Tablets for making  $\frac{1}{2}$  to  $\frac{1}{4}$ % solution for urethral injections and irrigations in gonorrhœa

**Novargan (Heyden, Dresden; Braun, London)** Silver proteinate containing 10% of silver.

**Argenti Proteinæ Mite (B P C.).**

*Syn. and Prop Names* ARGENTO-PROTEINUM MITE, ARGENTI NUCLEINAS, ARGENTI VITELLIN, ARGENTUM VITELLINATUM (*P. Belg IV*), PLATA VITELINA (*F E VIII*), ARGENTUM PROTEINICUM MITE (*U S P XI*), MILD PROTARGIN, ARGYROL (*Barnes, Philadelphia, Fassett & Johnson, London*) (20% Ag, also in solution-tablets containing 0.5 g), ARVITIN (*Johnson & Sons, London*) (20% Ag, with egg yolk protein), CARGENTOS (*Sharp & Dohme, London*) (20 to 25% Ag, with casein), LUNARGEN (*Lilly, London*) (20% Ag).

*Note.*—The name Mild Silver Protein is given to this group of compounds because, although containing more silver than the strong silver protein compounds, they are less bactericidal, and also less irritant

A brown powder or nearly black scales or granules containing 19 to 25% of Ag.

**Soluble** slowly but readily in water, almost insoluble in alcohol, chloroform and ether.

**Incompatible** with cocaine hydrochloride, but compatible with 1% atropine sulphate

**Uses.** Is used for the same purposes as silver protein but in stronger solutions, especially where irritation must be avoided. For corneal ulcers and as a spray for the nose and throat may be used up to 50% strength

In purulent conjunctivitis (gonorrhœal, neonatorum, etc.), free instillation of 25% solution every 3 or 4 hours, catarrhal conjunctivitis, 5 to 20% 1 or more times daily, trachoma, 25% solution rubbed with force on wool into lids once daily; dacryocystitis, 25% solution. For gonorrhœa may be used in various strengths up to 20% Pessaries for vaginitis may contain 5 to 10%

Ulcerative colitis has been treated by washing out with  $1\frac{1}{2}$  pints of 1% solution at 80°F.

**[P1] Guttæ Argyrolis cum Adrenalina (Mid H)**

Argyrol 25 gr, solution of adrenaline hydrochloride 20 m, glycerin 15 m, water to 1 oz Three drops into each nostril night and morning in acute or chronic sinusitis.

**Unguentum Argenti Proteinatis Mitis** 2% with paraffin basis in eczematous conjunctivitis and keratitis

**Silver Gelatose.** *P.G. VI* (15% Ag), *P. Svec. X* (16%).  
*Prop. Name.* ALBARGINE (*Bayer Products, London*).

According to the patent specification, gelatose (produced by hydrolysis of glutin, etc., by acid or alkali) 10 g., is dissolved in water 10 ml. and mixed, after neutralising, with silver nitrate 1.5 g. in water 5 ml. The mixture is evaporated to dryness *in vacuo*. The salt thus obtained is a yellow-white powder soluble to the extent of 50% in water.

A non-irritant compound containing 15% of silver, of sand-like appearance. **Soluble** about 1 in 2 of water, and about 1 in 130 of alcohol 90%. For gonorrhœa a 0.2% solution injected 4 or 5 times daily, or irrigation with 1 to 4000 solution. 0.5 to 3% for ophthalmic use. In bacillary dysentery silver gelatose injection is of great value—not in amœbic cases.

**Incompatible** with chlorides and tannin.

**Stains on fabric** may be removed with hot sodium thiosulphate solution 1 in 10.

### Silver Gelatose Enema.

**Dose.**—1 pint increased to 1½ pints of strength 1 gr. per oz on successive days.

**Argochrom** (Napp, London) A methylene blue and silver compound containing 20% silver Supplied in powder or solution as an antiseptic

**Protosil** (Parke, Davis, London) A combination of colloidal silver with an albuminoid Contains about 20% of silver Used in solution for treatment of inflammatory conditions of the mucous membranes

**Targesin** (Goedecke, Berlin) A diacetyltannin silver albumen combination in scale form, containing 6% of Ag 1 to 5% aqueous solutions for irrigation in gonorrhœal infections in the male and 6 to 10% in the female 5% ointment issued for inflammatory eye affections, and for ulcers and skin affections Tablets containing 0.25 g are made for internal use in gastritis, to be taken 4 times daily

**Argentum Colloidale** (*P. Helv V, P.G. VI, Fr. Cx. Supp 1926, P. Ned V, P. Svec. X, P. Jap V*) *Syn. and Prop Names* ARGENTUM CRÉDÉ, PLATA COLOIDAL (*F.E VIII*), COLLARGOL (*Heyden, Dresden, Braun, London*).

A preparation of silver in combination with protein, containing at least 70% of Ag (*P. Ned V 74.5 to 80%, P. Svec 72 to 80%*) In green or bluish-black plates with metallic lustre and bitter metallic taste.

**Soluble** slowly 1 in 2.5 of water; insoluble in organic solvents. Aqueous solutions should be freshly made as required and filtered

**Incompatible** with dilute mineral acids and concentrated salt solutions. In the latter case the precipitate dissolves on diluting with water.

**Uses.** For local treatment in the form of solution or ointment, 1 to 15%. For ophthalmic use 1 to 10% solutions are employed Diphtheritic membrane is said to disappear under swabbing with 5% solution. Intravenously, 2 to 10 ml of ½ to 2% solution for septic affections such as endocarditis and in difficult labours where septic complications feared. Orally as a ½ to 1% solution or in pills for gastric and intestinal catarrh.

**Suppositories of Collargol** 2½ grains, also [*P1 81*] **Compound Collargol Suppository.** Collargol 2½ gr., ethylmorphine hydrochloride ¼ gr., extract of cannabis 2 gr., glycerin and cacao butter q s In pelvic suppurations with pain, tenderness and general septic symptoms.

**Unguentum Crédé.** Collargol 15, white wax 10, benzoinated lard 75. For eczema, syphilis and gonorrhœa, and as a prophylactic to gonorrhœal ophthalmia

**Collosol Argentum** (*British Colloids, London*) Preparations of colloidal silver Solution (1 in 2000, dose—1 drachm) for intestinal affections, and applied topically for septic wounds and all inflammatory or suppurative conditions. Also prepared for injection in septicæmia and for ophthalmic use in conjunctivitis, etc **Collosol Argentum Beta** is a 1 in 400 solution, to be diluted with warm water or saline for use as a vaginal or rectal injection. Other preparations available are bougies, tampons, suppositories, ointment, paint (pigmentum) and oil.

**Choleval** (*Merck, Darmstadt, Martinsdale, London*) A compound of colloidal silver and sodium cholate. In powder, tablets, bougies and vaginal tablets. In gonorrhœa and as prophylactic

**Cryptargol** (*Lumière, Lyons; Anglo-French Drug Co., London*) A silver derivative of thioglycerin sulphonate of sodium, containing 35% of Ag. Supplied in pills or syrup for internal use as a gastro-intestinal antiseptic, and as a concentrated (10%) solution for external use as a general antiseptic and for use in dermatology, urology and gynecology Also as ovules (in vaginitis, metritis, etc.) and as collyria (1% and 5%)

**Cuprocollargol** (*Heyden, Dresden, Braun, London*). Electrocolloid copper silver solution containing 0.05% Cu and 0.05% Ag Dose—5 to 20 ml intravenously daily or every other day In septic conditions, puerperal diseases, septic abortion, etc

**Ichthargen** (*Cordes, Hermann, Hamburg*). Silver compound of ichthylol containing 30% of silver.

**Neo-Reargon** (*Norgine, Prague, Napp, London*) Compound of silver and anthraquinone glycosides containing about 14% of Ag For urethral injection in gonorrhœa in 1.5 to 2.5% solution, and for vaginal irrigation in 1 to 2% solution

## ARSENUM

As = 74.91

[P1] "Arsenical substances, the following, except those specified in Part II of this List.—Arsenic, halides of, oxides of arsenic; arsenates, arsenites; organic compounds of arsenic."

[P2] "Arsenical substances, the following.—Arsenic sulphides, arsenious oxide; calcium arsenates, calcium arsenites, copper acetarsenites; copper arsenates; copper arsenites; lead arsenates; potassium arsenites; sodium arsenates; sodium arsenites; sodium thioarsenates"

[81] "Arsenical poisons except substances containing less than the equivalent of 0.01% of arsenic trioxide"

[83] "Arsenical poisons—in pyrites ores or sulphuric acid containing arsenical poisons as natural impurities"

[86] "Arsenical poisons—specify proportion as the proportion of arsenic trioxide ( $As_2O_3$ ) or arsenic pentoxide ( $As_2O_5$ ) that the preparation would be calculated to contain on the assumption that the arsenic (As) in the poison had been wholly converted into arsenic trioxide or arsenic pentoxide as the case may be."

[P2-81] **Arseni Trioxidum** (B.P., U.S.P. XI, P. Dan.). Syn. ACIDUM ARSENIOSUM, ARSENIC, WHITE ARSENIC, ARSENIOS ANHYDRIDE, ARSENIOS ACID, ARSENIOS OXIDE, ACIDUM ARSENIOSUM (P. Helv. V).  $As_2O_3$  = 197.86.



**Dose.**— $\frac{1}{80}$  to  $\frac{1}{4}$  grain (0.001 to 0.005 g.). *U.S.P. XI* average dose  $\frac{1}{30}$  grain.

Maximum single dose  $\frac{1}{4}$  grain (0.005 g.); maximum daily dose  $\frac{1}{2}$  grain (0.016 g.). Possible fatal dose 2 grains.

Made by roasting arsenical ores. It occurs in white lumps or powder, and is usually a mixture of two varieties, one of which is opaque and crystalline and the other transparent and vitreous. The latter slowly changes to the former.

**Soluble** very slowly about 1 in 65 of water (*B.P.*). The solubility varies with the relative proportion of the two varieties present, the vitreous being more readily soluble than the crystalline. With some samples the solubility is not more than about 1 in 100. More soluble in water acidified with hydrochloric acid and in alkaline hydroxide and carbonate solutions. Soluble about 1 in 8 of glycerin; slightly soluble in alcohol 90%.

**Incompatible** with iron salts, lime water and magnesia

**Antidotes.** Empty stomach by emetic, or by stomach tube, using 2 gallons of water to which has been added precipitated ferric hydroxide (2 oz. of solution of ferric chloride, add sodium carbonate till effervescence ceases, filter and use precipitate). Give 4 oz. of arsenic antidote *B.P.C.*, repeating the dose if necessary. (If this is not available, give 1 oz. of tincture of ferric chloride in 4 oz. of water with 1 oz. of sodium bicarbonate added; or give magnesia mixed with water freely.) Keep patient warm. Give castor oil or saline purgative (magnesium sulphate). Demulcent drinks freely. Stimulants, *e.g.*, caffeine sodium benzoate, 2 gr hypodermically, may be necessary for collapse, or morphine,  $\frac{1}{2}$  gr. hypodermically, for pain. Saline infusion if required.

For use of sodium thiosulphate and sodium hydrosulphite in arsenical poisoning *see p. 104*

**Antidotum Arsenum** (*B.P.C.*, *P. Helv. V*, *P. Dan.*). *Syn* FERRI HYDROXIDUM CUM MAGNESII OXIDO *F.E. VIII* and *P. Jap.* use ferric sulphate, and in other pharmacopœias

**Dose.**—4 ounces (120 ml.).

Contains freshly precipitated ferric hydroxide and light magnesium oxide.

**Magma Ferri Hydroxidi** (*U.S.P. XI*)

**Average dose**—4 ounces (120 ml.).

Arsenic antidote kept ready for use in two parts (1) 40 ml. of solution of ferric sulphate diluted to 125 ml., (2) 10 g. of magnesium oxide or 300 ml. of Magma Magnesiae diluted to about 750 ml. in a 1000 ml. bottle. The two are mixed for use.

**Toxicology.**

Overdosage with arsenic is indicated by vomiting and diarrhoea, numbness and tingling in the feet, followed by muscular cramps and the development of anæsthetic areas in the limbs.

An interesting résumé in a paper on "The Relationship of Medicine and Toxicology" of numerous *causes célèbres* in which arsenic and antimony have been found. In one instance arsenic, given apparently for poisoning, was found in the hair to the extent of  $\frac{1}{2}$  mg. in 3 g. of hair—Sir William Willcox, *Lancet*, 1/1923, 167.

In criminal cases of arsenical poisoning the symptoms may be those of acute arsenical poisoning, such as one would expect from a single dose, masked

by those of prolonged action of arsenic. Thus, symptoms of arsenical neuritis or renal or liver disease may be superimposed upon those of the acute gastrointestinal symptoms.—Sir William Willcox, *Brit med. J.*, ii/1922, 118; *Lancet*, ii/1922, 129, 139.

Arsenic can be found months or years after taking, in the nails and hair — Sir W. Willcox, *Med Pr*, Nov 12, 1930

Stoke-on-Trent arsenic in sweets trouble. No deaths, probably because of the large amount of arsenic, 77 to 150 gr. in the lb of sweets. It was used as dusting powder and got into the treacle. It was originally bought by colour manufacturers, who left it on the premises where the sweets were made — *Brit med. J.*, ii/1930, 492

**Uses.** It is given internally immediately after meals as a general tonic and nerve tonic, as for chorea, in diabetes and anæmia, as antiperiodic for malaria, in association with iron, which it appears to render more easily assimilated, and for chronic skin diseases. Small doses of antimony may succeed when arsenic fails—especially in lichen planus. A short course of arsenic frequently clears up a superficial dermatitis. In exophthalmic goitre 5 minim doses of *Liquor Arsenicalis* thrice daily have been given for several months with one week's interval per month. It is said to increase respiratory power (Styrian mountaineers add it to their diet) and to improve the complexion. All preparations of arsenic should be given after food. Externally it has a caustic action, and is put into the cavities of carious teeth to kill the nerves.

In certain types of nervous vomiting in childhood, in obstinate cases, small doses of arsenic and opium, just before meals, are often immediately efficacious.

[D P1 81] *Gossypium Arsenii* (R D H) ARSENIUS WOOL.

Arsenic trioxide 5 parts, tannic acid 2 parts, morphine acetate 10 parts, liquefied phenol sufficient to make a thin paste. Mix with a sufficiency of finely cut cotton wool. Used in the same way as *Pasta Arsenicalis*. Some formulæ contain creosote instead of phenol.

[P2 81] *Granula Dioscoridis* (P Dan and Fr Cx)

Contains 1 mg of arsenic trioxide

Dose — 1 to 5

[P2 81] *Liquor Arseni Acidus* (B.P.C.) Syn *LIQUOR ARSENICI HYDROCHLORICUS*.

Dose — 2 to 8 minims (0.12 to 0.5 ml.) Contains 1% of arsenic trioxide in hydrochloric acid and water. Is compatible with acid mixtures.

[P2 81] *Liquor Acidi Arsenosi* (U.S.P. XI)

Average dose — 3 minims (0.2 ml.)

Contains 1% of arsenic trioxide and 5% of dilute hydrochloric acid; it resembles *Liquor Arseni Acidus*, B.P.C.

[P1 81] *Liquor Arseni Alkalinus* (B.P.C.)

Dose — 2 to 8 minims (0.12 to 0.5 ml.)

Contains 1% of arsenic trioxide, dissolved with the aid of potassium carbonate and coloured with compound tincture of lavender.

**Incompatible** with *Liquor Strychninæ Hydrochloridi*. Employ *Liquor Arsenicalis*. Poisoning has occurred.

[P2 81] *Liquor Arsenicalis* (B.P., Fr. Cx., P.G. VI, P. Jap., P. Belg. IV, F.E. VIII). Syn. FOWLER'S SOLUTION.

Dose. — 2 to 8 minims (0.12 to 0.5 ml.). Fr. Cx. gives max. dose during 24 hours, 25 minims approx.

Contains the equivalent of 1% of arsenic trioxide in neutral solution. The oxide is dissolved in potassium hydroxide and neutralised with dilute hydrochloric acid. The solution contains no compound tincture of lavender (*see* *Liquor Arseni Alkalinus*).

[P2 81] *Liquor Potassii Arsenitis* (*U S P XI*)

*Average dose.*—3 minims (0.2 ml.).

The same strength as *Liquor Arsenicalis, B.P.*, but prepared with potassium bicarbonate and alcohol instead of potassium hydroxide and hydrochloric acid, and therefore alkaline in reaction. Resembles *Liquor Arseni Alkalinus (B.P.C.)* but is colourless.

[P2 81] *Liquor Arsenicalis Glycerinatus* (*A P.F.*).

Heat arsenic trioxide 87½ gr. with glycerin 2 oz. to 150° to dissolve. Cool, add water 17 oz., then compound tincture of lavender 288 m. and water to 1 pint.

Solutions of arsenic trioxide in dilute glycerin are liable to give a very slight deposit of a crystalline form of  $As_2O_3$  on standing for 2 to 3 months.

SKIN PAPILLOMA well treated by swabbing thrice daily with the *B.P.* solution—*Per J. Amer. med. Ass.*, 1/1926, 654.

ARSENICAL KERATOSIS FOLLOWED BY CANCER Patient had a more or less general psoriasis, which was controlled by arsenic for 7 years. Warty growths appeared on palms and soles, and the arsenic was stopped. 14 years after cessation of the drug, the hyperkeratosis on palms and soles was as obvious as ever, and a tumour, necessitating amputation developed—*H. C. Semon, Brit. med. J.*, 11/1922, 975.

VINCENT'S ANGINA. Arsenic is specific, full doses of the *Liquor Arsenicalis* may be given three-hourly, or it may be used as a paint with glycerin.—*E. Watson-Williams, Practitioner*, 1/1936, 47. *See also* *Pigmentum Ipecacuanhæ et Arsenici*, p. 599.

[P2] *Mistura Antimalarica* (*Baccelli*) (*P Ital V*) *Dose*—¼ to 1 ounce (15 to 30 ml.).

Quinine sulphate 3 g., iron and potassium tartrate 7.5 g., distilled water 300 g., Fowler's solution 25 drops.

[P2] *Mistura Arseni Quininae et Ferri*. *Syn.* BACCELLI'S MIXTURE (slightly modified).

*Dose.*—¼ to 1 ounce (15 to 30 ml.)

Dissolve quinine sulphate 3 in water 150 with aid of a little dilute sulphuric acid. Then dissolve green ammonio-citrate of iron 5 in water 150, mix and add Fowler's solution 3. Employed in malaria.

[D P1 81] *Pasta Arsenicalis* (*B.P.C.*).

Arsenic trioxide 2 and morphine hydrochloride 1, mixed to a paste with creosote. *R.D.H.* is similar but uses morphine acetate.

The equivalent of about ⅛ grain of arsenic trioxide is sufficient.

Apply as follows:—Remove as much carious tissue as possible, exclude moisture and disinfect. Apply the paste as near pulp as possible and protect by concave cap. Seal cavity carefully with mastiche in chloroform.

[P2 81] *Caustiscin* (*Wölm, Spangenberg; Saccharin Corporation, London*). Arsenical caustic combined with a local anæsthetic for devitalising dental pulp. Prepared in three different strengths—"Blue," in the form of lamellæ, contains 40%  $As_2O_3$ —has powerful action and should be left for 24 hours only, "Yellow," in thread form, contains 30% of  $As_2O_3$ —slower in action and may be left for 3 to 5 days; "Black," in the form of lamellæ, contains slow and mildly acting metallic arsenic (40%  $As$ ), used particularly for milk teeth.

[P2 81] *Pilula Acidi Arseniosi et Ferri Redacti*.—MONCKTON.

*Dose.*—1 to 3 grains. Arsenic trioxide 12 gr., reduced iron 1 oz., excipient q.s.

[P1 81] *Pilula Arsenicalis et Strychninae* contains ½ grain (0.0013 g.) of each.

[P2 81] *Pilulae Asiaticae* (*B.P.C.*). *Dose.*—1 or 2 daily.

Each pill contains arsenic trioxide ⅛ gr. (0.005 g.) and black pepper ¼ gr. (0.05 g.). In chronic skin affections.

In psoriasis this is a convenient method of giving arsenic.

*P.G. VI* contains  $\frac{1}{4}$  gr. (0.001 g) of arsenic trioxide, and  $\frac{1}{2}$  gr. (0.03 g.) of pepper.

[P2 81] **Tablets of Arsenic, Iron and Quinine** contain arsenic trioxide  $\frac{1}{10}$  gr., ferric hypophosphite 2 gr., quinine acid sulphate 1 gr.

[P2 81] **Tablets of Arsenious Acid and Mercuric Chloride**  $\frac{1}{4}$  gr. (0.001 g) of each. In exophthalmic goitre have been given thrice daily

[P1 81] **Liquor Potassii Arsenatis et Bromidi (B.P.C.).**

*Syn.* CLEMENS' SOLUTION, LIQUOR ARSENII BROMIDI.

*Dose.*—2 to 8 minims (0.12 to 0.5 ml.), once or twice a day

A solution containing potassium arsenate and potassium bromide equivalent to 1% *w/v* of  $As_2O_3$  and 0.5% *v/v* of bromine.

The solution is useful in epilepsy and diabetes, with careful diet.

[P1 81] **Arseni Triiodidum (B.P., U S P. XI).**

*Syn.* ARSENII IODIDUM, ARSENIOS IODIDE.  $AsI_3 = 455.7$ .

*Dose.*— $\frac{1}{8}$  to  $\frac{1}{4}$  grain (0.004 to 0.016 g.), in a pill. *U S P XI* average dose  $\frac{1}{16}$  grain

The two elements combine, forming orange-coloured crystals. It should be recrystallised so as to exclude a melted mixture of elementary arsenic and iodine, or powdered arsenic 10, may be mixed with iodine 51 in presence of water, digested at gentle heat and evaporated to dryness

**Soluble** 1 in 11 of water, forming a slightly cloudy acid solution, 1 in 40 of alcohol 90%.

Solution 1% in 1 to 10 drop doses in milk, useful for lymphatic and scrofulous children, has marked iodine effect. Also used externally

It is of use in diseases of the alimentary canal, especially gastritis, in phthisis, and in all cases of neuritis.

[P1 81] **Injectio Arseni Iodidi.**

*Dose* — $\frac{1}{100}$  grain (0.0006 g) in 6 minims (0.4 ml.) of sterile water. The strength may be increased if desired.

[P1 81] **Liquor Arseni et Hydrargyri Iodidi (B.P.).**

*Syn.* DONOVAN'S SOLUTION.

*Dose.*—5 to 15 minims (0.3 to 1 ml)

Contains arsenic triiodide and mercuric iodide, of each 1%

Given for syphilitic skin diseases.

**Incompatible** with potassium iodide and sal volatile (*cf.* Nessler's reagent), also with alkaloids and acids.

Should be *freshly prepared* or stored in small bottles completely filled. A sample after 14 months was found to contain no arsenous arsenic.—*T. Tusting Cocking, Quart. J. Pharm., 1929, 409.*

**DISSEMINATED SCLEROSIS** Most neurologists consider arsenic the most useful drug. 10 to 12 m. of Donovan's solution in  $\frac{1}{4}$  oz. of water may be taken regularly thrice daily for months. Tincture of belladonna 10 m. may be added if there is faulty control of the bladder.—*Macdonald Critchley, Med. Pr., 1/1936, 520*

[P2 81] **Cupri Arsenis.**  $Cu_3As_2O_8 = 438.6$  *Syn.* SCHEEL'S GREEN.

*Dose.*— $\frac{1}{100}$  to  $\frac{1}{2}$  grain (0.0006 to 0.0025 g.)

Amorphous green powder, used in various intestinal affections, cholera morbus, cholera infantum, diarrhoea, dysentery and typhoid. *Dose* for adults  $\frac{1}{100}$  to  $\frac{1}{50}$  grain every 10 minutes for an hour, then hourly, for children, half this quantity. Small repeated doses essential. For chlorosis and functional anæmia  $\frac{1}{10}$  to  $\frac{1}{5}$  grain thrice daily are given.

[P2-81] **Potassii Arsenis.** *Dose.*— $\frac{3}{8}$  to  $\frac{1}{8}$  grain (0.002 to 0.004 g.). The dry salt,  $KAsO_3 \cdot HAsO_3 \cdot H_2O = 272.0$ , containing about 73% of  $As_2O_3$ , made from arsenious acid and potassium bicarbonate. Used occasionally in place of arsenious anhydride

[P2-81] **Sodii Arsenis.** *Syn* SODIUM METARSENITE  $NaAsO_2 = 129.9$

*Dose.*— $\frac{1}{8}$  to  $\frac{1}{4}$  grain (0.001 to 0.004 g.)

A whitish powder soluble in water, slightly in alcohol. Has properties equivalent to those of arsenic trioxide

[P1-81] **Sterules of Arsenic and Iron** (*Martindale, London*) are prepared in two strengths. No. 1 *grade (weak)* contain in 1 ml 0.025 g of soluble iron arsenite, equivalent to 0.0005 g of  $As_2O_3$ . No. 2 *grade (double strength)* contain the equivalent of 1 mg of  $As_2O_3$  per ml. *Dose*—15 minims (1 ml). For hypodermic injection in anæmia, etc. [P1-81] **IRON AND ARSENIC DROPS** for oral use contain soluble iron arsenite equivalent to 1 mg of  $As_2O_3$  per ml. *Dose.*—5 minims gradually increased to 20 minims

[P1-81] **Acidum Arsenicum** (*B.P.C.*) *Syn* ORTHO-ARSENIC ACID

$H_3AsO_4 \cdot \frac{1}{2}H_2O = 151.0$ .

*Dose.*— $\frac{1}{8}$  to  $\frac{1}{4}$  grain (0.001 to 0.005 g.).

A crystalline powder soluble about 2 in 1 of water, and very soluble in alcohol 90%. Arsenites are said to be twice as active as arsenates. The following salts are in use—

[P1-81] **Ferri Arsenas** (*B.P.C., Fr. Cx., F.E. VIII*)

*Dose.*— $\frac{1}{8}$  to  $\frac{1}{4}$  grain (0.004 to 0.016 g.) *Fr. Cx.* has *max. single dose*  $\frac{3}{4}$  grain, *max. in 24 hours*  $2\frac{1}{4}$  grains, *F.E. VIII* gives  $\frac{1}{2}$  grain and  $\frac{1}{2}$  grain respectively

This is an amorphous greenish powder and consists of ferrous and ferric arsenates and iron oxide, the ferrous iron content being equivalent to not less than 10% of  $Fe_3(AsO_4)_2$ . The ferrous arsenate rapidly oxidises in the air. In chronic skin affections of all kinds. Tablets contain  $\frac{1}{8}$  grain (0.008 g.)

[P1-81] **Ferarsin** (*Richter, London*) Iron arsenate  $\frac{1}{4}$  gr., strychnine nitrate  $\frac{1}{4}$  gr calcium glycerophosphate  $2\frac{1}{4}$  gr. *Dose*—1 or 2 tablets daily. Asthenic conditions, anæmia, etc

[P2-81] **Sodii Arsenas Anhydrosus** (*B.P.C.*)

*Syn.* SODIUM ARSENATE, DISODIUM HYDROGEN ARSENATE

$Na_2HAsO_4 = 185.9$ .

*Dose.*— $\frac{1}{10}$  to  $\frac{1}{5}$  grain (0.0015 to 0.006 g.)

Sodium arsenate crystallises with 7 or with 12 molecules of water. The former,  $Na_2HAsO_4 \cdot 7H_2O = 312.0$ , is included in *I.A., Fr. Cx., P. Ned. V., P. Helv. V., P. Belg. IV., P. Ital. V., and P. Dan.* *Fr. Cx.* has *max. single dose*  $\frac{1}{4}$  grain; *max. during 24 hours*,  $\frac{1}{2}$  grain approximately

The anhydrous salt, in white powder, dried at  $150^\circ$ , contains 61.8% of  $As_2O_3$ . 1 of the anhydrous salt equals 1.68 of the salt with  $7H_2O$ .

**Soluble** 1 in 6 of water. Slightly soluble in alcohol.

ULCERATIVE ENDOCARDITIS. Influence of arsenic (as sodium salt) advised—*J. Lycett, Brit. med. J., ii/1922, 402*

DEAFNESS. Sodium arsenate has been found beneficial,  $\frac{1}{2}$  grain in pill followed by  $\frac{1}{4}$  grain the next day—altogether 40 to 60 pills in as many days—*Per Pharm. J., ii/1926, 287*

[P1-81] **Injectio Sodii Arsenatis et Strychninae.**

*Dose.*—5 to 10 minims (0.3 to 0.6 ml.) hypodermically

Sodium arsenate 2 ( $\frac{1}{8}$  gr. in 10 m.), strychnine hydrochloride 1 ( $\frac{1}{8}$  gr. in 10 m.), water to 600.

[P1-81] **Sterules of Sodium Arsenate and Strychnine** (*Martindale, London*) contain 10 m. of the above injection.

[P1 81] **Injectio Sodii Arsenatis et Strychninae et Quininae** contains 1 gr. of quinine acid hydrochloride added to 10 m. of the above

[P2 81] **Liquor Sodii Arsenatis (B.P.C.)**.

*Dose*.—2 to 8 minims (0.12 to 0.5 ml.). 1% of the anhydrous salt.

[P2 81] **Pearson's solution of arsenic** used on the Continent, *e.g.* *P Ital V* is 1 of crystallised sodium arsenate ( $7H_2O$ ) in water 600, *P Belg IV* is 1 in 1000

## ORGANIC ARSENIC COMPOUNDS

An organic arsenic compound, as distinct from the inorganic form, has the arsenic in combination with a carbon atom. This appears to lessen its toxic properties. Furthermore, arsenum acts either as a tri- or penta-valent element and, broadly, the former compounds are more potent upon protozoa. Examples of the first class are arsphenamine and of the second, sodium cacodylate, sodium arsanilate, tryparsamide, etc. The compounds are classified below under the headings (i) *Aliphatic*, (ii) *Aromatic*, (iii) *Diphenyl nucleus* bodies, as far as practicable.

### (I) Aliphatic Series.

[P1 81] **Acidum Cacodylicum (B.P.C.)**

*Syn* DIMETHYLARSONIC ACID  $(CH_3)_2AsO \cdot OH = 138.0$

*Dose* —  $\frac{1}{2}$  to 2 grains (0.03 to 0.12 g.)

The ultimate product of oxidation of cacodyl, tetramethyldiarsine,  $(CH_3)_2As-As(CH_3)_2$ , discovered by Bunsen in 1842, and of cacodyl oxide, *n* alkarsin,  $(CH_3)_4As_2O = 226.0$ . Colourless hygroscopic crystals neutral to methyl orange, acid to phenolphthalein.

**Soluble** about 2 in 1 of water, 1 in 4 of alcohol 90%, readily in chloroform.

Although containing 54.3% of As, equivalent to 71.6% of  $As_2O_3$ , it is relatively non-toxic—similarly with the salts. It will be noted that this acid has only 1 OH group, hence it is not so toxic as its parent arsonic acid, with 3 OH.

Sodium cacodylate and disodium methylarsonate are probably broken down in the body to such slight extent that large doses may be given without producing any therapeutic, much less toxic, effect. They appear, principally in the urine, unaltered. A small proportion is, however, oxidised, and from this arsenic ions are set free, exerting a mild action during a prolonged treatment.

[P1 81] **Calcii Cacodylas**.  $[(CH_3)_2AsO_2]_2Ca = 314.0$ .

*Dose* —  $\frac{1}{2}$  to 2 grains (0.03 to 0.12 g.) *per os* or intramuscularly.

A white amorphous powder. **Soluble** 2 in 1 of water, 1 in 2 of alcohol. In tuberculosis daily injections of  $\frac{1}{2}$  grain, with a glycerin solution of calcium iodide 10 grains and ferrous iodide  $1\frac{1}{2}$  grains per drachm internally, have been found satisfactory.

[P1 81] **Trophil (Napp, London)**. Organic calcium-arsenic compound for subcutaneous injection. Ampoules contain 1 ml. Also supplied in combination with strychnine nitrate.

[P1 81] **Ferri Cacodylas.**  $[(CH_3)_3AsO_2]_3Fe = 466.8$ .

**Dose.**— $\frac{1}{4}$  to  $\frac{1}{2}$  grain (0.016 to 0.03 g.) *per os* three times daily, up to 5 grains *per diem* may be given. Intramuscularly  $\frac{1}{2}$  to  $1\frac{1}{2}$  grains (0.03 to 0.1 g.) *per diem*. Intravenously 1 grain (0.06 g.) in 5 ml.

**Manufacture.** Precipitate the ferric hydroxide from a sufficiency of ferric chloride solution containing 1 molecular proportion of ferric chloride ( $Fe_2Cl_6 + Aq.$ ). Wash the precipitate and combine with cacodylic acid 6 molecular proportions.

Yellowish powder soluble 1 in 15 of water. Used for anæmia and chlorosis, also in glandular swellings, *e g.*, in syphilis, hypodermically.

Iron cacodylate  $\frac{1}{2}$  grain intravenously every other day used for raising the hæmoglobin content.—H. Pritchard, *Brit med J*, 1/1927, 794.

[P1 81] **Ferruginous Ampoules** (*Frasse, Paris; Wilcox, Jozeau, London*) contain iron cacodylate 0.01 g ( $\frac{1}{20}$  grain), sodium glycerophosphate 0.1 g. ( $1\frac{1}{2}$  grains) and strychnine cacodylate 0.0005 g ( $\frac{1}{2000}$  grain) in 1 ml. **Dose**—1 ml subcutaneously or intramuscularly daily for 12 days.

[P1 81] **Drops** containing the above quantities in 25 minims are prepared.

**Dose**—8 to 10 drops in water after food twice a day (for adults). Maximum daily dose 25 drops.

[P1 81] **Iron-Arsenic-Strychnine Compound G.L.** (*Glaxo Laboratories, London*) is a preparation in ampoules for injection as a tonic and in anæmia.

[P1 81] **Guaiacol Cacodylas.**  $(CH_3)_3AsO \cdot O \cdot C_6H_4(OCH_3) \cdot H_2O = 262.0$

**Syn.** CACODYLIACOI

**Dose.**— $\frac{1}{2}$  to 2 grains (0.03 to 0.12 g.) *per os* or hypodermically in sterile oil in affected regions for tuberculosis. Soluble 1 in 25 of water, 1 in 15 of alcohol 90%.

[P1 81] **Magnesi Cacodylas.**  $[(CH_3)_3AsO_2]_2Mg \cdot 2H_2O$

**Dose.**— $\frac{1}{2}$  grain (0.05 g.) hypodermically, gradually increased (5% solution suitable). White amorphous powder soluble 1 in 3 of water.

**Uses, etc.,** as the sodium salt, *q v*

[P1 81] **Sodii Cacodylas** (*B.P.C., P. Helv. V, Fr. Cx. and Supp 1920, P.G. VI, U.S.P. XI, P. Ital. V, F.E. VIII, P. Belg IV*)

**Syn.** SODIUM DIMETHYLARSONATE.  $(CH_3)_2AsO_2Na \cdot 3H_2O = 214.0$

**Dose.**— $\frac{1}{4}$  to 1 grain (0.016 to 0.06 g.) orally, *per rectum* or hypodermically. When given orally an alliaceous odour is imparted to the breath; the odour is less marked when the compound is given by injection.

**Fr. Cx.** has max. single dose 3 grains and max. during 24 hours 3 grains approximately. **P. Helv. V** has  $1\frac{1}{2}$  and 5 grains respectively for oral administration and 3 and 10 grains respectively for hypodermic injection.

A white, odourless, crystalline or granular powder, very deliquescent.

The salt of the above formula contains 35% of As whilst the anhydrous salt contains 46.8%, equivalent to 61.8% arsenious acid. **P.G. VI** requires a content of 32.8 to 35% of As. **Fr. Cx. Supp 1920** gave a formula with  $2\frac{1}{2}H_2O$  (previously anhydrous) and stated the official salt must contain 75 to 78% of anhydrous sodium cacodylate. (Not confirmed in 1926 *Supp.*). **P. Ital IV** requires it to contain 70%. **U.S.P. XI** requires 72 to 75% of  $(CH_3)_2AsO_2Na$ . In commerce it usually contains 18 to 25% of water.

**Soluble** 2 in 1 of water, 1 in 1 of alcohol 90%.

**Uses.** In tuberculosis generally (curative results come very slowly), in diabetes mellitus, exophthalmic goitre, pernicious

anæmia, cancer (particularly of the stomach), malaria, chorea, leprosy, psoriasis and other chronic skin affections, and in all cases in which arsenic has been used, but when given by the mouth or per rectum may cause renal congestion with albuminuria and fall in the quantity of urine excreted.

As far back as 1862 cacodylic acid was found to give excellent results in treatment of chronic skin diseases and in pulmonary tuberculosis. It was stated in 1865 (before Koch's discovery of the bacillus) to "impart to the blood of the patient a condition inimical to the tuberculosis." Much later it was employed in syphilis and for the various other purposes for which arsenic is indicated.

The usual dose in syphilis is 1 to 2 gr. intramuscularly *per diem* for a week or 10 days. Some prefer 3 gr. daily for 7 days, then 1 gr. doses subcutaneously. Similar dosage has been used in paralysis agitans.

**CHILBLAINS** Sodium cacodylate injections  $\frac{1}{2}$  grain. Three injections at intervals of about two days good.—W R Grove, *Lancet*, 1/1926, 312.

**BRONCHO-SPIROCHÆTOSIS, CHRONIC**, rapidly recovered under sodium cacodylate *per os*—E C Faust, *J trop Med (Hyg)*, 1923, 14.

**DISSEMINATED SCLEROSIS** Good results with  $\frac{1}{2}$  gr doses injected daily or every other day for 12 to 14 days. The patient was kept fit for 18 months with injections at 3-monthly intervals.

**ENDOCARDITIS** treated by Capps's sodium cacodylate method. Daily intravenous injections beginning with 1 grain and increasing gradually to 5 grains. Free from ill effects.—Sir Thomas Horder, *Brit med J*, 1/1926, 737.

**FURUNCULOSIS** Sodium cacodylate hypodermically on alternate days rapidly clears up furunculosis.—B. Ghosh, *per Prescriber*, 1928, 324.

**MALARIA** well treated by intravenous injections of 30 gr., divided into 4 doses of 7½ gr. at 6-hour intervals, until parasites have disappeared from peripheral blood, when dose is halved and continued for a fortnight.—*J Amer. med Ass*, 11/1926, 124.

**PEMPHIGUS** of acute type responded dramatically to 2 gr doses. Total injected 50 gr during 5 weeks.—L. J A Loewenthal, *Brit med J*, 1/1930, 153.

**PERNICIOUS ANÆMIA** Sodium cacodylate  $\frac{1}{2}$  gr may be given hypodermically daily for 20 days.—Sir W H Willcox, *Lancet*, 11/1927, 778.

**SEPTICÆMIA** Arsenic, e.g., sodium cacodylate, intramuscularly, may be placed first—given in conjunction with nucleic acid, usually 1 gr. of sodium cacodylate in a saturated solution of nucleic acid, 1 ml intramuscularly being given twice in 24 hours for the first two or three weeks of an acute case. A good leucocyte stimulant. A convenient method of knowing that the patient is receiving an effective dose is the smell of his breath.—Sir Thomas Horder, *Brit med J*, 1/1925, 657, *ibid*, 11/1931, 593.

[P1 81] **Elixir Sodii Cacodylatis.** Dose— $\frac{1}{2}$  drachm (2 ml.)

Sodium cacodylate  $\frac{1}{2}$  gr., simple elixir to  $\frac{1}{2}$  dr. This forms a palatable method of administering the salt.

[P1 81] **Injectio Sodii Cacodylatis.** A sterile preparation containing the equivalent of 0.05 g ( $\frac{1}{2}$  grain) of cacodylic acid in 1 ml (15 minims approx.) The same dose diluted with 4 drachms of water is used for rectal injection.

[P1 81] **Sterules of Sodium Cacodylate and Nucleic Acid** (*Martindale, London*) contain 1 gr. of sodium cacodylate in 1 ml. of nucleic acid solution (*vide Acidum Nucleicum*).

[P1 81] **Injectio Cacodylatum Compositum.** Dose (average)—15 minims (1 ml.), containing sodium cacodylate  $\frac{1}{2}$  gr., iron cacodylate  $\frac{1}{2}$  gr., strychnine cacodylate  $\frac{1}{2}$  gr. It should be rendered slightly acid with cacodylic acid. 1 ml contains approx. 0.03 g. ( $\frac{1}{2}$  gr.) of As.

Gautier recommends [P1 81] cacodylic acid 5 g., sodium carbonate q.s., cocaine hydrochloride 0.08 g., creosote 6 drops, dissolved in alcohol 8 g. with



sterile water *q.s.* to 100 ml, *i.e.* 15 minims (1 ml.) contain  $\frac{1}{2}$  grain (0.05 g.) of cacodylic acid for a dose—hypodermically—which is not to exceed 0.1 g (1½ grains) *per diem* the average being 0.02 to 0.05 g. every 24 hours

[P1 81] **Cyto-Sol** (*Corbière, Paris, Anglo-French Drug Co., London*) Ampoules of 5 ml. contain sodium cacodylate 0.3 g, strychnine sulphate 0.001 g in isotonic saline. Dose—5 ml intramuscularly or intravenously daily or every other day

[P1 81] **Hemo-Cyto-Sol** (*Corbière, Paris, Anglo-French Drug Co., London*) Colloidal iron 0.01 g, sodium cacodylate 0.3 g, strychnine sulphate 0.001 g, isotonic saline 5 ml Dose—5 ml intramuscularly daily or every other day

[P1 81] **Optarson** (*Bayer Products, London*). Solution of ammonium heptin-chlorarsenate and strychnine nitrate Dose—1 ml subcutaneously (= 0.004 g of  $As_2O_3$  and 0.001 g. of strychnine nitrate). Tonic

[P1 81] **Strychninæ Cacodylas.**

$C_{21}H_{22}N_2O_2 \cdot (CH_3)_2AsO OH = 472.2$ .

Dose.— $\frac{1}{30}$  to  $\frac{1}{10}$  grain (0.002 to 0.006 g), usually by injection

White crystalline powder hardly soluble in water, readily soluble in chloroform Has proved a useful salt.

[P1 81] **Sérum Névrossthénique Ampoules** (*Fraisse, Paris, Wilcox, Jozeau, London*) contain 0.1 g of sodium glycerophosphate and 0.0005 g of strychnine cacodylate, for hypodermic injection In neurasthenia and other nervous affections Dose—1 ampoule daily for 12 days

[P1 81] Drops are also prepared for use by the mouth, containing the above quantities in 25 minims. Dose—25 drops daily

[P1 81] **Di-sodii Methylarsonas** (*F.E. VIII, P Ital. V*)

*Syn and Prop Name.* SODIUM METHYL ARSONATE, SODIUM METHARSINITE, ARRHENAL (*Adrian, Paris*), "NEW CACODYLE"

$AsO(CH_3)(ONa)_2 \cdot 6H_2O = 292.0$  Fr. Cx and P Belg IV have  $5H_2O$

Dose.— $\frac{1}{2}$  to 2 grains (0.03 to 0.12 g) *per os* or hypodermically Fr. Cx. has max. single dose and max in 24 hours 3 grains

Prepared by the interaction of methyl iodide and sodium arsenate in presence of excess of alkali In white crystalline powder containing (with  $6H_2O$ ) 25.65% of As

**Soluble** about 1 in 1 of water, only slightly in alcohol 90%

**Uses.** Similar to Sodium Cacodylate, *q.v.*

It is stated not to produce cacodyle oxide when given by the mouth

[P1 81] **Enesol** (*S E M P.A., Paris, Mertens, London*), is MERCURY SALICYLARSONATE, a combination of disodium methylarsonate and mercury salicylate. A white powder containing 36% mercury. It is best supplied in solution. This is said to be painless on injection

Dose.— $\frac{1}{4}$  to 1 grain (0.015 to 0.06 g.) intramuscularly.

Syphilis and parasyphilis are treated by 2 ml of 3% solution (= 1 grain approx.) intramuscularly once daily, or for intensive treatment of syphilis 4 to 8 ml every 2 or 3 days. Intravenously, 4 to 10 ml. every 2 or 3 days according to urgency When a total amount of 1.5 g is reached, treatment should be suspended for 10 days.

General paralysis, malaria, and psoriasis, are also treated with it

[P1 81] **Sterules of Mercury Salicylarsonate** (*Martindale, London*) contain 1 gr in 30 m

[P1 81] **Araylen** (*Hoffman-La Roche, London*) Allylarsonic acid. In granules containing 0.01 g. in the form of calcium allylarsonate, or ampoules containing 0.05 g. as sodium allylarsonate. In skin and blood diseases, convalescence, etc.

[P1 81] **Arsamon** (Heyden, Dresden, Braun, London) A solution of sodium monomethylarsonate for subcutaneous or intramuscular injection in anæmia 1 ml = 0.05 g. of As.

[P1 81] **Tetrasthenol** (Modern Pharmaceuticals, London) Contains methylarsonates of iron, sodium and strychnine, with iron glycerophosphate and sodium chloride. *Dose*.—3 ml subcutaneously For neurasthenia, anæmia, etc

## (II) Aromatic Series

[P1 81] ***p*-Aminophenylarsonic Acid**. *Syn* ARSANILIC ACID, ANILINE-ARSENIC ACID.  $\text{NH}_2\text{C}_6\text{H}_4\cdot\text{AsO}(\text{OH})_2 = 217.0$ .

Arsanilic acid is weakly basic. Its hydrochloride is immediately hydrolysed by water. It is soluble, however, in methyl and ethyl alcohols. It has been employed as—

[P1 81] **Sodii Aminarsonas**  $\frac{1}{2}$ (B.P.C.). *Syn. and Prop. Names*. SODIUM *p*-AMINOPHENYLARSONATE, SODIUM ARSANILATE, ARSAMIN (Martindale, London), ATOXYL (Bayer Products, London), SOAMIN (Burroughs Wellcome, London).  $\text{NH}_2\text{C}_6\text{H}_4\text{AsO}(\text{OH})\text{O Na} = 239.0$ . Contains a variable proportion of water, usually 3 to 4 molecules. *P Belg. IV* requires  $3\text{H}_2\text{O}$ . *B.P.C.* requires 24 to 25.6% of As.

*Dose*— $\frac{1}{4}$  to 3 grains (0.05 to 0.2 g). This dosage *per os* for syphilis has been advised daily for a week, then to be intermitted, but caution is recommended. Max single dose 3 grains (0.2 g).

*Intramuscular injections* (into the buttock) have been given of much larger doses, even up to 10 grains at a time, in a total course of 100 grains, at several days' interval in treatment of syphilis. The upper third of the buttock is the usual site of injection.—*N.B.* Not without danger—Avoid heroic doses.

*Intravenously* 1 to 5 minims (0.06 to 0.3 ml) of a 15% solution have been given, *i.e.* approx.  $\frac{1}{4}$  to  $\frac{1}{2}$  grain, but larger doses have been used. At least 1 ml of diluent is desirable.

Solutions should be freshly prepared with cold boiled water and may be slightly warmed at time of injection.

A white crystalline powder with slightly saline taste.

**Soluble** about 1 in 6 of water (some samples may dissolve in a little less). Also soluble about 1 in 125 of alcohol 90% and more so in methyl alcohol. The anhydrous substance is readily soluble in methyl alcohol but practically insoluble in ether, acetone, benzene or chloroform.

**Incompatible** with mercurials (*e.g.*, perchloride), and other heavy metals in solution, also with acids.

**Uses.** Large quantities of arsenic were formerly given by this means in skin diseases (psoriasis, lichen), in anæmia, syphilis, sarcoma, elephantiasis, malaria and tuberculosis. Syphilis has been treated with 50% ointment used on chancre of the skin. It is, however, no longer used in syphilis either internally or externally owing to the danger of causing optic neuritis and atrophy. It is given only in those conditions where small amounts of arsenic are effective.

It is stated to have less than  $\frac{1}{15}$  the toxicity of arsenic trioxide.

It has also been given in cases of disseminated sclerosis and tabes without bad effects, but cases must be watched carefully.

**Elimination** of sodium aminarsonate is by the skin and the kidneys. May cause transient albuminuria, the bulk is in the urine. The excretion usually amounts to 50 to 90% within 9 hours. The amount remaining is to some extent decomposed, so that sometimes toxic symptoms of inorganic arsenic are produced. Fortescue Brickdale thought there was no advantage in giving in syphilis and anæmia a rapidly eliminated form of arsenic in large dose, rather than one which being slowly excreted can be given in small doses.

[P1 81] **Pills of Sodium Aminarsonate** contain  $\frac{1}{2}$  grain and upwards

[P1 81] **Sodium Aminarsonate Paste**, 10%, may be prepared with **Pigmentum Caseinæ**, q v.

In syphilis this has been used to primary sores, with large injections of sodium aminarsonate simultaneously into the buttock

[P1 81] **Sodii Acetylarsanilas** (P. G. VI, P. Belg. IV).

*Syn. and Prop. Name.* SODIUM ACETYLAMINOPHENYL-ARSONATE, ACETYL-ATOXYL (Boehden, Berlin)

$C_6H_4 \cdot NHCOCH_3 \cdot AsO_3HNa, 4H_2O = 353 \cdot 1$ . P. Helv V has  $5H_2O$ .

*Dose.*—Per os  $\frac{1}{2}$  grain (0.03 g.) 3 or 4 times a day.

Colourless crystals. **Soluble** 1 in 10 of water, insoluble in alcohol.

In syphilis, malaria, trypanosomiasis. A course of 20 injections of 0.6 g. spread over 10 weeks. In the case of diseases of metabolism smaller amounts—0.1 to 0.3 g.

*Caution.*—This dosage is quoted in Gehe, but blindness has been reported after its use.

P. G. VI states maximum single dose 0.2 g. P. Helv. V approx. 4 grains; maximum by injection  $1\frac{1}{2}$  grains.

Specially recommended in pernicious anæmia, leukæmia and lymphadenoma—*Brit. med J. Epit.*, 11/1924, 63.

[P1 81] **Acetarsol** (B. P. Add.). *Syn. and Prop. Names.* ACET-ARSONE, 3-ACETYLAMINO-4-HYDROXYPHENYLARSONIC ACID, STOVARSOL (Pharmaceutical Specialties (May & Baker) Ltd, London), KHAROPHEN (Burroughs Wellcome, London), ORARSAN (Boots, Nottingham), SPIROCID (Bayer Products, London).

$CH_3 \cdot CONH C_6H_3(OH)AsO(OH)_2 = 275 \cdot 0$ .

*Dose.*—1 to 4 grains (0.06 to 0.25 g.) for adults;  $\frac{1}{2}$  grain (0.03 g.) maximum for children. Stated to be readily absorbed from the gastro-intestinal tract

Colourless crystals having a high As content (27% approx.) and low toxicity. It was introduced by Fourneau and Levaditi in 1922.

**Insoluble** in cold water, alcohol 90% and dilute acids; moderately soluble in boiling water and in alkalis, the corresponding salt being formed.

**Toxic symptoms** sometimes occur, e.g., diarrhoea, vomiting, headache and cutaneous eruptions.

Exfoliative dermatitis due to continued use—J. C. Michael, *J. Amer. med. Ass.*, 1/1929, 645.

One tablet of Stovarsol (0.25 g.) taken immediately after breakfast made a man violently ill. Copious draughts of warm water, also a ferric hydrate mixture

produced recovery. Symptoms were suggestive of arsenic poisoning.—J. R. O'Brien, *Lancet*, 1/1926, 313.

Dermatitis, from administration of 40 gr. in 13 days, quickly subsided on giving 10 ml intravenous injections of a 10% strontium bromide solution (Ekzebro) —H. C. Semon, *Lancet*, 11/1932, 341.

Toxic erythema in 13, and peripheral neuritis in 2, out of 232 cases of amœbiasis treated. Risk of treatment considerable and particularly dangerous unless patient is under constant supervision —P. W. Brown, *J. Amer. med. Ass.*, 11/1935, 1321.

**Uses.** In amœbiasis, frambœsia (yaws), lambliasis, malaria (*Plasmodium Vivax*) and the early treatment of syphilis. Has the advantage of being active when given orally.

Used with success in spirillary diseases, e.g., intestinal spirochætosis, ulcer-membranous-stomatitis, spirillary bronchitis, phagedenic ulcer, and Vincent's angina, also lesions resistant to arsphenamines.

In acute cases of amœbiasis destruction of cysts entails dosage of 8 gr per day for 10 days. Stated to cure when emetine has failed. In chronic cases, 4 gr the first day, later 4 gr. every other day for a week, then twice a week for several weeks. (For the combined treatment with Auremetine, v. p. 605.)

The combined treatment of amœbic dysentery (in France) with acetarsol and emetine lasts 4 weeks and consists of administration of 0.5 g. of acetarsol a day during 1st and 3rd weeks, and emetine during 2nd and 4th weeks. The "opening" treatment with acetarsol alone consists of administration of 0.75 g. a day for one week, discontinued following week and resumed on 3rd week, followed for one or two months by daily dose of 0.25 g. Amœbæ disappear in 4 days and cysts in 8 days. Affects *Lamblæ* but *Trichomonas* resists it. Superior to neoarsphenamine.

In FRAMBŒSIA (yaws) the following has been advised. Two 4 gr tablets the first day, three the second day, four the third day. Omit for one day, then four, three and two tablets respectively on alternate days. For lambliasis, one 4 gr tablet a day for six days. The dose may be doubled and treatment extended, in cases with cysts. The dosage for children should be *pro rata*. Improvement with disappearance of cysts. Blastocysts, the cause of diarrhœa, destroyed.

In malaria 15 gr. *per os*, in a single dose, will free the blood of tertian parasites but does not affect malignant or quartan forms. It is said to be a useful adjuvant to quinine.

NEUROSYPHILIS —Good results reported from intravenous injection of Stovarsol. Solution prepared by dissolving 1 g. in 9 ml of 4% sodium hydroxide and adding 11 ml of distilled water. Initial dose 0.5 g. and succeeding doses 1 g. at weekly intervals —L. H. Griggs and J. F. Schamberg, *Arch. Derm. Syph.*, N. Y., 1934, 645.

RESPIRATORY DISEASES, CHRONIC, treated with doses of 0.5 g., given for 10 to 15 days, interrupted by intervals of equal duration. Hepatic or renal insufficiency are contraindications —*Brit. med. J. Ept.*, 1/1926, 48.

SYPHILIS well treated by 1 g. daily, with a total of 20 g. in the month. Bismuth in addition may be required. Has a general tonic action on the whole system. —C. Levaditi, *Lancet*, 11/1925, 594.

Congenital syphilis in infants of 2 months treated with a daily dose of 0.12 g. for 4 days a week up to a total of 6.6 g. —*Brit. med. J. Ept.*, 1/1926, 52.

**TICK FEVER.**—Stovarsol gave good results.—A. T. Schofield, *Brit med. J.*, ii/1927, 1140.

**VINCENT'S ANGINA** and ulcerating stomatitis treated—*Brit med. J Epit*, i/1928, 35.

[P1 81] **Acetarsol Sodium.** *Syn. and Prop. Name.* SODIUM ACETYLAMINOHYDROXYPHENYLARSONATE, STOVARSOL-SODIUM (*Pharmaceutical Specialties (May & Baker) Ltd, London*). A white powder soluble 1 in 8 of water

For injection in frambæsia (yaws), general paralysis, and malaria

Ampoules contain 0.5, 1 and 1.5 g, injections being given three times a week until a total of 20 g has been given

[P1 81] **Devegan Vaginal Tablets** (*Bayer Products, London*) Acetarsol and boric acid with carbohydrate hydrolysed by a special process. In leucorrhœa, especially that due to *Trichomonas vaginalis*

Review of results of 185 cases of vaginal discharge. Best results only obtained with in-patients. One to four tablets of Devegan inserted high in the vaginal fornices, at first twice daily and then at lengthening intervals, and finally just after the menstrual periods only. Desired result obtained in from 2 weeks to 2 months in two-thirds of the cases. Complete disappearance of discharge, or a substantial improvement, occurred in all but a small proportion of cases. Results definitely superior to antiseptic douches—P. Hauptstein, per *Lancet*, i/1936, 382

All but 7 of 47 patients clear of trichomonas infection after 3 months (and 5 of the 7 had an associated gonorrhœa). The tablets are more effectively inserted by an experienced person—J. L. Collis, *J Obstet Gynec*, Feb, 1936, 87

The best results in trichomonas vaginitis have been obtained by the use of Devegan tablets, 2 tablets, inserted once or preferably twice daily and used in conjunction with an alkaline or a 1 in 1000 potassium permanganate douche, have relieved the condition quickly. It must be realised, however, that unless treatment is continued for from two to three months relapses are almost certain to occur—E. W. Assinder, *Brit med J*, i/1936, 882

[P1 81] **Stovarsol Vaginal Tablets** (*Pharmaceutical Specialties (May & Baker) Ltd, London*) are used for similar purposes

[P1 81] **Hectine** (*Mouneyrat, Villeneuve-la-Garenne, Anglo-French Drug Co., London*) Sodium benzosulpho-*p*-aminophenylarsonate. For intramuscular injection or oral use in syphilis and filariasis

[P1 81] **Hectargyre** (*Mouneyrat, Villeneuve-la-Garenne, Anglo-French Drug Co., London*). A combination of Hectine with mercury, as an adjunct to the arsenical treatment of syphilis

[P1 81] **Bistovol** (*Pharmaceutical Specialties (May & Baker) Ltd, London*) Bismuth acetylaminohydroxyphenylarsonate, the bismuth salt of acetarsol, in ampoules containing 3 ml of 10% suspension in oil.

For adults a series of 12 injections of 1.5 to 3 ml at intervals of 4 to 5 days is suggested.

Acetarsol and sodium potassium bismuth tartrate interact, producing a white precipitate of this body. Has a curative effect both on animal and human syphilis. With mice, found of value for *Trypanosomiasis nagana*. In general, the ill-effects of bismuth or arsenic are not observed

Primary and secondary syphilis well treated by Bistovol *per os* either in solution or tablets. Well tolerated in doses of 2 g. daily for 8 to 11 days. Rapid disappearance of spirochetes and prompt cicatrization of lesions—C. Levaditi and L. Fournier, *Lancet*, i/1928, 697

[P1 81] **Acetylarsan** (*Pharmaceutical Specialties (May & Baker) Ltd, London*)

Diethylamine acetarsol, a white crystalline powder, soluble in water. Two solutions are prepared: (1) for adults, containing 23.6% of active product, 1 ml. of which is equivalent to 0.05 g. of arsenic; and (2) for children weighing less than 15 kg., containing 9.4% of active product, 1 ml. of which equals 0.02 g. of arsenic (the basis of dosage with this solution is 0.15 ml. per kilo body weight). It is given subcutaneously or intramuscularly, the dosage in adults (after two preliminary injections, one of 1 ml. and one of 2 ml.) being 3 ml. given at

three-day intervals, a course consisting of 16 injections with an interval of one month between courses. Alternatively 5 ml may be given, once a week for 8 weeks (not more than 3 ml at one site). Indicated in all stages of syphilitic infection, in neurosyphilis, congenital syphilis, and in yaws. Used in hepatitis with success—dose, 0.75 g once a week for 4 weeks. Also used, in conjunction with emetine, for amebiasis.

Effect on *S. pallida* equal to that of the arsenobenzenes, and serological effect compares favourably. More frequently followed by minor toxic effects than the arsenobenzenes—V. E. Lloyd, *Lancet*, 1/1928, 1323.

[P1 81] **Parosan** (*Pharmaceutical Specialities (May & Baker) Ltd, London*)

8-Acetyl-amino-3-hydroxy-1,4-benzisoxazine-6-arsonic acid. Has some analogy with Stovarsol and Tryparsamide. Tablets contain 4 gr. In disseminated sclerosis and neurosyphilis. Of little use in early syphilis.

[P1 81] **Acidum 4-Oxy-3-formylaminophenylarsinicum** (*P. Belg IV*). *Syn. and Prop. Name.* TREPARSOL (*Lecoq et Ferrand, Paris; Bengué, London*) (0.25 g tablets), FORMYPHENARSINE, FORMYL-*m*-AMINO-*p*-OXYPHENYLARSONIC ACID.

A white powder almost insoluble in water, alcohol and ether. For oral administration in syphilis.

[P1 81] **Carbarsone** (*Fli Lilly, London*) *p*-Carbamino-phenylarsonic acid,  $\text{NH}_2\text{CONH} \cdot \text{C}_6\text{H}_4\text{AsO}(\text{OH})_2$ .

Dose—0.25 g twice daily for 10 days in gelatin capsules.

A white crystalline solid first prepared by Ehrlich, without odour or taste, containing 28.85% of arsenic. It is practically insoluble in water, but dissolves in alkaline aqueous solutions and melts at 174°.

*Uses.*—In the treatment of amebiasis. It is stated to be less toxic than acetarsol, but more amoebicidal. Caution is advised until it is decided whether or not it may injure the eye. The arsenic is only slowly liberated and care must be taken to avoid arsenic toxicity.

It is non-toxic in clinically effective doses—A. C. Reed and co-workers, *J. Amer. med. Ass.*, 1/1932, 189-198. Apparently effective—*ibid.*, 231.

Study of forty-four drugs in order to find one with low toxicity and high amoebicidal powers showed Carbarsone to be the best. 0.25 g given twice daily for ten days. In obstinate cases retention enema of 2 g of Carbarsone in 200 ml of warm water with 1% of sodium bicarbonate, after preliminary cleansing, enema repeated on alternate nights for five treatments. No toxic symptoms—only slight epigastric discomfort reported—H. H. Anderson, *J. trop. Med. (Hyg.)*, 1/1933, 69.

Doses of 0.25 g of Carbarsone twice daily for 10 days with no untoward effects in 31 cases and with 23 cures reported by R. N. Chopra, B. and S. Sen, *Indian med. Gaz.*, 1933, 315.

200 ml enemas of 1% Carbarsone in 2% sodium bicarbonate last thing at night after a sedative of sodium Amytal, repeated until they have been retained on five occasions, of value when the oral use of the drug had failed. In extensive trials orally and rectally in total quantities of 75 to 2100 mg per kilo, over periods of up to 15 months, intolerance only noted in one case of hepatitis after 5 g in ten days—H. H. Anderson and J. C. Reed, *Amer. J. trop. Med.*, 1934, 257.

A total oral dosage of 3.0 g per kilo over a period of 48 weeks has been employed with no perceptible harm—H. A. Anderson, *J. trop. Med. (Hyg.)*, 1935, 272.

[P1 81] **Tryparsamidum** (*B.P. Add., U.S.P. XI*). *Syn.* SODIUM *N*-PHENYLGLYCINEAMIDE-*p*-ARSONATE (*P. Ital. V*), GLYPHENARSINUM (*P. Belg IV*), TRYPARSONUM (*B.P.C.*).

$\text{NaO}(\text{OH}) \cdot \text{AsO} \cdot \text{C}_6\text{H}_4 \cdot \text{NH} \cdot \text{CH}_2 \cdot \text{CONH}_2, \frac{1}{2} \text{H}_2\text{O} = 305.0$ .

The U.S. patent, owned by the Rockefeller Institute, having expired on September 24th, 1935, the Institute has dedicated the name tryparsamide to the public as a non-proprietary designation, and the Council on Pharmacy and Chemistry of the A.M.A. has adopted the name as a non-proprietary name for the product.—*J. Amer. med. Ass.*, 1/1936, 781.

In Canada tryparsamide is controlled by patents until November 2nd, 1938.

**Dose.**—15 to 30 grains (1 to 2 g.) by subcutaneous, intramuscular or intravenous injection. *U.S.P. XI average dose* 30 grains intravenously. Up to 45 grains may be given for a dose.

A white crystalline powder obtained by treating sodium aminarsonate with chloracetamide and recrystallising the sodium salt of the acid thereby obtained. The anhydrous substance contains about 25% of As. It is required to comply with biological tests for freedom from toxicity.

**Soluble** 3 in 10 of water, forming a neutral solution, almost insoluble in alcohol, chloroform and ether.

**Uses.** Originally introduced for the treatment of trypanosomiasis, but is effective only against *T. gambiense* (African sleeping sickness); *T. rhodesiense* is not destroyed. Is now used also in neurosyphilis and usually preferred to arsphenamine compounds in tabes and paresis. It is liable to produce optic atrophy, and is contraindicated in neurosyphilis with optic neuritis. Has no effect on primary or secondary syphilis. Should be given in courses of 8 or 10 weekly injections, the total dosage required being 20 to 40 g. in trypanosomiasis (more in chronic cases), and 130 g. or more in neurosyphilis. Injections are usually given intravenously. Toxic effects are indicated by ocular pain, lachrymation and photophobia.

**TRYPANOSOMIASIS.**—In patients of the first stage, a total dosage of 20 to 40 g. usually cures, but in chronic cases 50 to 100 g. is necessary (Van den Branden). The best dosage for adults in good condition is 3 g. weekly, and in poor condition 2 to 3 g.; for children 0.5 to 2 g. Action is rapid, durable, constant, and superior to any other drug, relapses or incomplete cures being due to extraneous causes; toxic reactions are negligible, cases of total blindness recorded being due to previous arsenical treatment (Marugo).

The single course of 50 g. for an adult appears to cure 52% and to ameliorate greatly 48% in the second stage. Accidents insignificant and ocular troubles rare and not severe (Infante).—Abstracts of papers on the use of tryparsamide, *per Trop. Dis. Bull.*, Oct., 1928, 790.

Results of use in 1000 cases. Exerts unique action on advanced cases, but equally satisfactory in early cases. A drug capable of oral use would be of benefit.—a German preparation called "4002" has given promising results experimentally *per os*—Louise Pearce, *Rockefeller Inst Monograph*, 1930; *Brit. med. J.*, 11/1930, 1094.

During 1934, 47,187 cases of sleeping sickness were treated in Nigeria, the great majority with a course of 20 to 25 g. of tryparsamide—initial dose 1 g., followed by 2 g. doses at 5-day intervals. Fewer toxic symptoms using distilled rather than boiled and filtered water. Antrypol (*see* p. 909) became available towards the end of 1934, and patients are now being given 3 doses each of 1 g. of Antrypol, followed by a course of 9 to 11 g. of tryparsamide,

with 5-day intervals between injections with both drugs.—H. M. O. Lester, *Report of the Tsetse Investigation*, per *Trop. Dis. Bull.*, 1936, 33, 169.

**NEUROSYPHILIS**—General condition of patients improved—sense of well-being.—D. Lees, *Brit. med. J.*, 11/1925, 14.

Marked serologic improvement in majority of cases of all types 50 or more injections are usually required over a period of a year or longer.—H. C. Solomon and H. R. Viets, *J. Amer. med. Ass.*, 11/1925, 331.

Neurosyphilis treated intravenously, and in some cases subcutaneously, in weekly doses of 3 g. in 10 ml. water over a period of 8 or 10 weeks. At the same time mercury salicylate intramuscularly in 1 grain doses. Reactions both early and late appear to have been considerable, including visual disturbance in 20% of cases. There was a good effect on nutrition.—J. D. Silverston, *Lancet*, 11/1926, 693.

**GENERAL PARALYSIS AND TABES**—In 20 cases treated at Maudsley Hospital no remarkable results were obtained. Similar improvements might have been obtained with other arsenicals.—W. S. Dawson, *Lancet*, 1/1925, 1072.

In general paralysis, particularly megalomaniac forms, the prolonged use is worthy of trial. 1 to 2 g. doses given at weekly intervals intravenously.—M. Brown and A. R. Martin, *Lancet*, 11/1926, 699. See also *J. Amer. med. Ass.*, 1/1927, 475.

The drug has no spirochæticidal effect in man but has a local stimulating effect on the nervous system. In 37 cases of general paresis there was clinical cure or marked improvement in 63%, and serological cure or marked improvement in 75%. Clinical improvement depends very largely on the duration of the parenchymatous involvement and the degree of pre-existing damage. Tryparsamide appears capable of arresting the active syphilitic process but not of undoing the damage done. Optic injury is rarely produced after the tenth injection, and early and repeated examination of the eye is therefore essential.—F. E. Cormia, *Brit. J. ven. Dis.*, 1934, 99.

[P1 81] **Biarsamide** (*Pharmaceutical Specialities (May & Baker) Ltd., London*) Bismuth tryparsamide, containing 14.5% As and 40.5% Bi. Ampoules contain 5 ml. 2% solution for intramuscular injection in nervous syphilis.

[P1 81] **Neocryl**. *Syn.* SODIUM SUCCINANILOMETHYLAMIDE-*p*-ARSONATE. A white crystalline substance readily soluble in water. Rather less toxic than tryparsamide and has greater trypanocidal activity. Well tolerated in man, by intravenous injection of a 15 to 20% solution in sterile distilled water, in weekly amounts of from 2 to 4 g., the usual course consisting of the administration of this amount weekly up to a total of 30 to 36 g., one patient had an uninterrupted course of 69 g. without showing toxic symptoms. Neocryl has a definite action on primary, secondary and tertiary syphilis, though in primary syphilis it is best combined with bismuth. In neurosyphilis and tabes it gave very satisfactory results, and of 11 cases of Nigerian trypanosomiasis treated by a single course, 10 became clinically normal and the other was improved.—Warrington Yorke and co-workers, *Brit. med. J.*, 1/1936, 1042 (Report to Therapeutic Trials Committee).

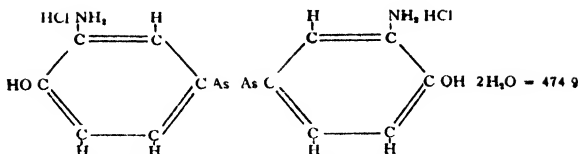
For an account of the preparation and therapeutic activity of succinyl derivatives of *p*-arsanilic acid see G. T. Morgan and E. Walton, *J. chem. Soc., Lond.*, March, 1931.

### (III) Diphenyl Nucleus Series

[P1 81] **Arsphenamina** (*B.P.C., U.S.P. XI*) *Syn. and Prop. Names.* ARSENOBENZENE, ARSENOBENZOL, ARSENPHENOL-AMINE, AMINO-ARSENO-PHENOL, ARSENOBILLON (*Pharmaceutical Specialities (May & Baker) Ltd., London*), DIOXYDIAMINO-ARSENOBENZENE DIHYDROCHLORIDE, SALVARSAN (*Bayer Products, London*) (*P.G. VI*), EHRLICH-HATA, or "606."

Arsphenamine consists mainly of the dihydrochloride of 3 : 3'-diamino-4 : 4'-dihydroxyarsenobenzene.





**Dose.**— $1\frac{1}{2}$  to 10 grains (0.1 to 0.6 g.), by intravenous injection  
*U.S.P. XI average dose 6 grains.*

**Therapeutic Substances Act, 1925**—Under this Act and the Statutory Rules and Orders issued under it in 1931 (*see p. 1036*), arspenamine, commonly known as *Salvarsan*, and analogous substances used for the specific treatment of infective disease, are controlled by Licence, under the Minister of Health in England and Wales, the Scottish Board of Health in Scotland, and the Minister for Home Affairs in Northern Ireland, both with regard to manufacture and standards of strength, quality and purity.

The Standard Preparations of arspenamine, etc., are kept in the National Institute for Medical Research, Hampstead. Biological tests and tests for stability are applied. The label must state that the contents have been tested in accordance with Regulations under the Act.

*Tests for Toxicity and Therapeutic Tests are described in Vol. II.*

**Introduction.** Ehrlich and his assistants (notably S. Hata of Tokyo) conducted research (*vide* "Die Experimentelle Chemotherapie der Spirillosen"), which led finally to the introduction of arspenamine for treatment of syphilis and other affections. It was hoped the compound would effect a "sterilisation of the system."

Arspenamine solutions kill protozoa *in vitro*, and the  $\frac{C}{T}$  ratio,

*i.e.*,  $\frac{\text{Curative dose or sufficient to destroy all parasites}}{\text{Toxic dose or max. dose which patient can tolerate}}$  for the substance is satisfactory. Ehrlich maintained that this ratio must be  $\frac{1}{2}$  or less for a drug to be of value in this type of disease.

**Note.**—The

$$\text{Chemotherapeutic Index (R)} = \frac{\text{M.T.D.}}{\text{M.C.D.}} = \frac{\text{Max. tolerated dose}}{\text{Min. curative dose.}}$$

If it is fairly large (5 to 10), the minimum curative dose is sufficiently far removed in quantity from the maximum dose tolerated for the drug to be useful.

**Manufacture.** *p*-Hydroxyphenylarsonic acid,  $\text{C}_6\text{H}_4\text{OHAsO}(\text{OH})_2$ , on nitration and subsequent reduction under certain conditions produces a condensation of two molecules forming ultimately the dihydroxy-diamino compound. This base is then converted into the dihydrochloride.

The varying toxicity of commercial samples is apparently due chiefly to presence of sulphonic derivatives formed during reduction process with sodium hyposulphite.

The compound forms a bright yellow powder, freely mobile in contact with glass surfaces, and odourless except for a slight smell of ether. Theoretically it contains approximately 31.6% of As. The Therapeutic Substances Regulations require not less than 30% or more than 34%. U.S.P. XI requires not less than 30% of As and it must comply with the requirements of the National Institute of Health, U.S. Public Health Service. It is available in ampoules, each containing 0.6, 0.5, 0.4, 0.3, 0.2 or 0.1 g filled with inert gas to prevent oxidation. If discoloured—either grey or brownish—it must not be used.

**Soluble** 1 in 5 of water, forming a thick syrupy liquid with acid reaction, but not acid to congo-red paper, 1 in 3 of methyl alcohol, 1 in 12 of ethyl alcohol, also soluble in glycerin. Insoluble in ether.

The dihydrochloride may be converted into the basic substance dihydroxydiaminoarsenobenzene (No. 592 in Hata's series) of the formula  $C_{12}H_{12}O_2N_2As_2$  by treatment with alkali. This base is an unstable, easily oxidisable, *insoluble* substance containing 40.98% of As—readily soluble, however, in alkalis.

### Toxic Effects and their Treatment.

Arsphenamine compounds in excess are all liable to damage capillary endothelium. In the dosage commonly employed a wide variety of toxic manifestations may occur. *Vasomotor symptoms* of an anaphylactic nature may occur during or immediately after the injection, and lasting for about 30 minutes, rarely longer. For treatment, 10 to 15 m. of adrenaline solution should be given subcutaneously. These toxic symptoms may be avoided by careful preparation of the solution and by slow administration.

*Rigor and headache*, diarrhoea and cramp in the legs may occur. They are usually due to faulty diet. All patients should fast for at least two hours before injection.

Late effects, including stomatitis, erythema, exfoliative dermatitis, headache, lassitude and possibly jaundice and cerebral disturbances may come on at periods varying from a few days to a few weeks. Stomatitis is more common in patients treated with mercury or bismuth in addition to arsenic. Headache and lassitude are indications for a break in treatment. For the dermatitis, sodium thiosulphate is given intravenously or intramuscularly (0.45, 0.6, 0.75 and 0.9 g.) on alternate days with 25 ml of 25% dextrose intravenously on each of the intervening days. 30 gr doses orally may also be given. Liver extract is also often very beneficial. Jaundice is rarely severe but may cause death. A high fat and high protein diet with low carbohydrate is useful for prevention. For treatment, intravenous injections of 25 ml to 50 ml. of 25% glucose should be given daily.

Some authorities recommend routine injection of sodium thiosulphate before treatment with arsphenamine compounds. More recently ascorbic acid (*q.v.*) has been used with success in the treatment of dermatitis due to arsphenamine.

Cerebral symptoms are rare but usually fatal. Prompt treatment by phlebotomy to 20 oz., removal of 15 ml. of cerebrospinal fluid, and injection of 1 ml. of solution of adrenaline may be successful, the lumbar puncture being repeated if symptoms continue.—L. W. Harrison, *Price's Practice of Medicine*, 4th Edn., 1934.

Atropine  $\frac{1}{4}$  gr. hypodermically is also advised for immediate vasomotor reactions. The cardiac reactions are best treated with hypodermic injections of strychnine  $\frac{1}{4}$  gr., ether 30 m, or camphor  $1\frac{1}{2}$  gr.—P Power, *J R Army Med Cps*, Jan., 1927, 46.

Toxic effects not due to arsenic content but to the amino-benzene derivatives. The 1922 Report of the M R C Salvarsan Committee needs revision —Semon, *Lancet*, 11/1931, 914.

**Contraindications.** Addison's disease, hæmophilia, severe visceral disease. Small initial doses and extra caution are necessary in alcoholism, cachexia, renal or cardiac lesions and where there is a tendency to eczema, also in diabetes since arsphenamine compounds increase the amount of blood sugar.

**Uses.** The acidity of arsphenamine must be neutralised at the time of use; it has been largely replaced by neoarsphenamine, which needs only to be dissolved in water when required for use. The compounds are similar in effect and the description of uses, etc., below applies also in a large measure to the latter.

Arsphenamine is usually given intravenously by the gravity method. Intramuscular injections, into the gluteal muscles, are now little used on account of the pain produced. Sulpharsphenamine has superseded it for that route.

A syphilitic chancre, a secondary syphilide or ulceration, or a tertiary gumma or ulceration, yields remarkably to the arsenicals. They are also of value in acquired or congenital syphilis, but in parasymphilitic affections they have not yet been proved of great benefit, though they may prevent their progress. Combined treatment with mercury or bismuth in addition is now more usual than treatment with arsenic alone.

Arsphenamine compounds are also used in malaria, septicæmia, relapsing fever, rat-bite fever, and yaws, also as a local application in Vincent's angina.

**Preparation of the Injection.**—Dissolve the dose in about 10 ml. of sterile water and make it alkaline by adding normal caustic soda solution (40 g. per litre), using the amount on the label required to dissolve the dose. A precipitate is formed which redissolves on shaking. Dilute with normal saline so that each 0.1 g. is contained in approx. 20 ml. of solution. Injection is usually through one of the veins of the fold of the elbow, e.g., the median cephalic, but any prominent vein may be used.

**Dose.**—0.1 to 0.6 g. Early syphilis is generally treated with from 0.2 to 0.3 g., and a number of injections, at intervals of a few days, gradually increasing up to 0.6 g., are given, with a total of 4 to 5 g. This course is usually repeated after an interval varying from 4 to 6 weeks, and three or four such courses are generally required. The injection should not be given immediately before or after a meal. A mild purgative before the injection lessens the liability to untoward reactions. Children may receive from 0.02 to

0.2 g., according to age, but sulpharsphenamine subcutaneously, or nearsphenamine intravenously, are preferable in such cases.

"Combined Treatment" with mercury, *vide postea*.

Patients should be treated in bed and observed for at least three days. If patient shows any signs of collapse during administration, the injection should be stopped at once.

### Combined Arsphenamine and Mercurial (or Bismuth) Treatment.

An analysis of records of 3598 cases treated at St. Thomas's Hospital V.D. Centre between January, 1920 and March, 1926.

A course consisted of not less than 5 g of an arsphenamine compound (except with silver arsphenamine, *q v.*) with a minimum of 5 gr. of mercury or 2 g. of bismuth, intramuscularly or subcutaneously, over a period of not more than 4 months. With silver arsphenamine a total of not more than 2.5 g was given, with or without mercury or bismuth. A second course was given 3 months after the first and completed in 4 months.

The results of treatment with arsphenamine compounds and mercury, compared with those with arsphenamine compounds and bismuth, showed no superiority of bismuth over mercury, though bismuth was better tolerated. (The preparation of bismuth used was mainly the oxychloride suspended in glucose solution.)

In sero-negative primary cases not less than two courses were necessary, and in sero-positive primary and early secondary cases even three courses did not give a satisfactory percentage of cures. Most relapses in early cases occurred in the first year, and a very small proportion after the second.

#### UNIT COURSE ON WHICH TREATMENT OF CASES ANALYSED IN REPORT WAS BASED

Day.	Arsphen- amine comp grammes	and Hg grains	or Bi grammes	Day	Arsphen- amine comp grammes	and Hg grains	or Bi grammes
1	0.45	—	—	50	0.75	1	0.4
8	0.45	1	0.4	57	0.75	1	0.4
15	0.45	1	0.4	78	0.75	1	0.4
29	0.60	1	0.4	85	0.75	1	0.4
36	0.60	1	0.4	92	0.75	1	0.4

(Potassium iodide from 57th to 78th day)

#### COURSE INSTITUTED 22/2/1928

In this course the principle is to follow three short "bursts" of "914" (which ought effectually to destroy accessible spirochaetes) with three rests of a month each to allow liver cells and skin to recover, and to finish with two full courses of "914". The bismuth is crowded into the first 10 weeks to build up a depot.

Day	Arsphen- amine comp gram- mes	Bi gram- mes	Day	Arsphen- amine comp gram- mes	Bi gram- mes	Day	Arsphen- amine comp gram- mes	Bi gram- mes
1	0.45	0.4	43	0.75	0.4	85	0.90	—
8	0.45	0.4	50	0.90	0.4	92	—	—
15	0.60	0.4	57	—	0.4	99	—	—
22	—	0.4	64	—	0.4	106	—	—
29	—	0.4	71	—	—	113	0.90	—
36	—	0.4	78	0.90	—	120	0.90	—

—Col. L. W. Harrison, "The Treatment of Syphilis," *Spec Rep. Ser med Res Coun, Lond*, 1929, No 132

Extra courses of arsphenamine, rather than mercury, for prevention of Wassermann reactions and destruction of residual spirochaetes Grey oil courses said to increase tendency to relapses —Prof E E Glynn, *Lancet*, ii/1926, 1075.

Modern aspects of syphilis Every early primary case with negative Wassermann reaction should receive 20–25 arsphenamine injections intravenously and some 16–18 of mercury and bismuth, or mercury given *per os* —W H Brown, *Brit med J*, ii/1926, 890

"Alternating" treatment economical and successful, whilst "Concurrent" is wasteful and productive of greater number of uncured syphilitics —E Tytler Burke, *Lancet*, i/1931, 1127

Adequate treatment of syphilis Further discussion —L W Harrison, Howard Allen and D Lees in reply to Col Burke, *ibid*, 1265

First place given to "606"—hits the spirochaete harder and longer than "914" in dosage equivalent in terms of arsenic, but reactions deterred many patients from continuing The sulpharsphenamine class subcutaneously better than "914" intravenously, but often painful and more likely to cause aplastic anaemia More "914" used in the clinic, but more sulpharsphenamine in private cases Mercury reserved for cases in which bismuth is impracticable Calomel best, the pain being obviated by use of anæsthetic vehicle If pain was not tolerated, use mercurial cream (not greater than 10% strength) —Col L W Harrison, *Brit med J*, ii/1931, 157

**Syphilis Treatment** (*Quart Bull Hlth Org L o N*, 1935, 1, 239).

An enquiry in five countries (Denmark, France, Germany, Gt Britain and the U S A ), carried out under the auspices of the Health Organisation of the League of Nations, into the treatment of syphilis in selected clinics. Statistical material was obtained from 94 clinics with 25,623 cases The experts concerned in the enquiry (and subsequent recommendations) were J. Jadassohn, Th Madsen, L W Harrison, L Queyrat, J H Stokes, H. Gougerot, Svend Lomholt, H Westergaard, and H Martenstein As a result of the enquiry the following recommendations were made —

1. Treatment as early as possible in the sero-negative primary stage. The fullest possible use should be made, for the purposes of diagnosis, of the microscopical examination of secretions from primary lesions or from lymph glands

2. Prior to treatment, there should be an adequate physical examination to determine the absence or otherwise of any indication for caution in dosage.

3 In carrying out the treatment, a strict supervision of the patient should be exercised, especially in respect of mucous membranes, skin, kidneys and liver

4. Observations, clinical and serological, after completion of treatment should be for not less than three years.

5. Adequate examination of the spinal fluid, at least before dismissal from observation, is essential

6. The principles to be followed in carrying out the actual treatment should be as follows (a) To employ a comparatively heavy individual dosage of the arsenobenzene and of the bismuth or mercurial compounds, the doses being administered in comparatively rapid succession, especially at the commencement, (b) to maintain a persistent attack on the disease, avoiding intervals of such length as to afford the parasite an opportunity of recovering;

(c) to administer approximately as much treatment to primary as to secondary cases.

A system either of intermittent treatment or of continuous treatment can be expected to yield satisfactory results in ordinary cases of early syphilis

#### PLAN OF INTERMITTENT TREATMENT

##### 1 Males

For adult males of average weight aged less than 50 years and in whom there is no contraindication. At the beginning of this course, some administer at once the full weekly dose (0.6 g. to 0.75 g.), whilst others divide it into two doses (e.g., 0.30 g. and 0.45 g.) so far as the first week is concerned

Week	"914"	"606"	Insoluble compound of bismuth* containing Bi metal
1st	0.6 to 0.75 g	or 0.4 to 0.5 g	and 0.20 to 0.24 g
2nd	" "	"	" "
3rd	" "	"	" "
4th	" "	"	" "
5th	" "	" "	" "
6th	" "	"	" "
7th	" "	"	" "
8th	" "	"	" "
9th	"	" --	0.20 to 0.24 g
10th	—	--	0.20 to 0.24 g

\* (1) By *insoluble* bismuth is here meant compounds of a very slight solubility in water. The dosage of all bismuth compounds should be calculated according to their content in bismuth metal

(2) As an alternative to bismuth, a course of mercury may be given, either in the form of inunctions (40 days at 3 g. of *Unguentum Hydrargyri*) or of injections (70 mg. of calomel or 120 mg. of mercury salicylate, etc., suspended in a suitable base)

It is recommended that (a) In cases which remain or become serologically negative during, or by the end of, the first course, four such courses be administered, with intervals of three to five weeks between any two courses, (b) in cases which have not become sero-negative by the end of the first course, in addition to the amount of treatment shown in (a), further courses should be administered until the patient has received as a minimum three beyond that which has ended with negative serum reactions. At the option of the individual clinician, this treatment may be prolonged as may be considered necessary (c) cases presenting signs of clinical relapse of an early type should be dealt with on principle similar to those enunciated in (b)

##### 2. Females.

For females (non-pregnant), treatment should be administered on the plan outlined for males, with the exception that the single dose of "914" should be reduced by 0.15 g. and that of "606" by 0.1 g

In the event of any reduction in the amount of treatment being indicated, it is recommended that this be effected by reducing the number of arsenical injections rather than by reducing the individual dose or increasing the interval

PLAN OF ALTERNATING CONTINUOUS TREATMENT FOR  
EARLY SYPHILIS

Day or week	"606" grammes	Interim treatment	Serol test	Remarks
Day				
1	0.3-0.6	—	1	<p>"606" dosage for first three injections at level of 0.1 g. for each 25 pounds (11.3 kg) body weight. Average subsequent dosage 0.4 g. men, 0.3 g. women, the fourth and subsequent injections in the first course at weekly intervals. In average patient all lesions heal rapidly and blood serological reaction becomes negative during first course. If "606" cannot be used, substitute 8 to 10 doses 0.3 g. silver arsphenamine (silver salvarsan, etc.), or 10 to 12 doses "914" (0.45-0.6 g. maximum for women and 0.6-0.75 g. for men). This applies also to subsequent courses.</p> <p>If mercury is used, note overlap of one week at end of first and start of second "606" courses. At this point a few days without treatment may be dangerous. Neuro-relapse.</p> <p>"606" starts, bismuth stops. Watch for provocative serological reaction after first dose of "606".</p> <p>Try to prevent short lapses in treatment, especially at this early stage.</p> <p>Bismuth is better than mercury. Use it if possible. Examine cerebrospinal fluid if patient's co-operation can be secured at about this time. If found to be abnormal, continue or intensify treatment as required, re-examining fluid within six months.</p>
5	0.3-0.6	—	—	
10	0.3-0.6	—	—	
Week				
3	0.4	—	—	
4	0.4	—	—	
5	0.4	—	—	
6	0.4	—	—	
7	0.4	—	1	
8	—	Bismuth 4 doses,	—	
9	—	0.2 g., and KI,		
10	—	or Ung Hydrarg		
11	—	and KI		
12	0.4	—	1	
13	0.4	—	1	
14	0.4	—	—	
15	0.4	—	—	
16	0.4	—	—	
17	0.4	—	1	
18-23	—	Bismuth 6 doses (or Ung Hydrarg.) and KI	—	
24	0.4	—	—	
25	0.4	—	—	
26	0.4	—	—	
27	0.4	—	—	
28	0.4	—	—	
29	0.4	—	—	
30-37	—	Bismuth 8 doses (or Hg) and KI	—	
38	0.4	—	1	
39	0.4	—	—	
40	0.4	—	—	
41	0.4	—	—	
42	0.4	—	—	
43	0.4	—	1	

Day or week.	"606" grammes	Interim treatment	Serol. test	Remarks.
44-53	—	Bismuth 10 doses (or Ung Hydrarg ) and KI	—	Note that bismuth or mercury courses are gradually getting longer—four, six, eight, and now ten weeks.
54	0.4	—	1	The average sero-negative, sero-positive primary or early secondary patient should have at least five courses of "606"
55	0.4	—	—	
56	0.4	—	—	
57	0.4	—	—	
58	0.4	—	—	—
59	0.4	—	1	
60-69	—	Bismuth 10 doses (or Ung Hydrarg ) and KI	—	It is safer to finish treatment with bismuth or mercury rather than with "606"
70-122	Probation	No treatment	6-12	
123	Complete physical and neurological examination, lumbar punctures, and, if possible, fluoroscopic examination of heart and great vessels			

As an optional scheme, three series of ten to twelve injections each of the arsenical drugs may be given. To secure an overlapping of the heavy metal and the arsenical, believed by some observers to protect against neuro-relapses, begin the bismuth two, three, or even four injections before the end of the longer arsenical course, continue it through the period in which the arsenical is suspended, and on into the beginning of the next arsenical course. The bismuth is then suspended while the arsenical course is completed.

The bismuth salt advised is bismuth salicylate in oily suspension, in full adult dosage with due regard for weight. Other preparations of bismuth may be used only with due regard for an equivalent metallic content and for their rate of elimination. The mercurial inunction is 50% metallic mercury in a suitable fatty base, dose 4 g. per inunction, five to six inunctions per week. The use of the iodide is optional, depending on indications.

The use of insoluble mercurials intramuscularly in this system is not recommended.

It should be further understood that, when heavy metal is employed after the last "606" course, the heavy metal courses are to be separated by rest intervals of 6 to 8 weeks between each series of 10 weeks' injections, or each course of forty inunctions.

In cases of primary syphilis which have remained sero-negative throughout, a minimum of five courses of "606" or "914" should be given. Cases of sero-positive primary syphilis should receive the full treatment called for by this system.

**NEURO-SYPHILIS.** Defined as comprising only such nervous or mental symptoms as are actually due to the syphilitic organism



or its toxin. It does not mean the mere presence of nervous or mental symptoms in a syphilitic patient. The treatment is arsphenamine combined with mercury, but 0.6 g of the former intravenously is now considered risky. It is safer to give not more than 0.3 g in repeated doses. *Salvarsanised serum* (patient's own blood), or human or horse serum mercurialised *in vitro*, is suitable for tabes and cerebrospinal syphilis. Arsphenamine given direct intraspinally into the cerebrospinal fluid is dangerous.—Sir J. Purves-Stewart, *Brit med J.*, 11/1922, 621. See also S. A. Kinnier Wilson, *ibid*, 628. See also D. K. Adams' "Treatment of Neuro-syphilis with special reference to changes in the cerebrospinal fluid," (cell counts and colloidal gold reaction, *ibid*, 630).

**Arseno-Solvent** (*Laboratoire de Biochimie Médicale, Paris, Modern Pharmaceuticals, London*) Chloretone 0.5, guaiacol 0.5, dextrose 5.0, water to 100. A solvent for various arsphenamine compounds, supplied in ampoules containing 2 ml.

[P1 81] **Eparseno** (*Société Paristenne d'Expansion Chimique, Paris*) is stated to be a stabilised solution of arsphenamine for painless injection in the treatment of syphilis, yaws, recurrent fever, etc. It is supplied in ampoules each containing 1 ml of solution, corresponding to 0.12 g of arsphenamine or 0.25 g of neoarsphenamine.

[P1 81] **Stabilarsan** (*Boots, Nottingham*) A stable compound of arsphenamine and glucose for intramuscular or intravenous injection supplied ready for use, as an approximately 10% solution in 50% glucose. Ampoules contain 0.05, 0.1, 0.15, 0.20, 0.30, 0.45, 0.6, 0.75 and 0.9 g. Doses larger than 0.45 g should not be given intramuscularly.

In congenital syphilis the preparation is stated to be safe. For an infant 15 lbs weight dose 0.075 g (0.75 ml of the solution in the ampoule). For routine treatment of syphilis a course is given combined with potassium iodide on the lines of arsphenamine methods. Has also been used with success in Vincent's angina, disseminated sclerosis and lymphadenoma.

[P1 81] **Sanogyl** (*Villette, Paris, Sealand Trading Ltd, London*) A tooth-paste to combat pyorrhœa, claimed to have a specific action on spirilla of the mouth, and to contain arsphenamine.

[P1 81] **Arsphenamina Argentica** (*B P C*) *Syn and Prop Name.* SILVER ARSPHENAMINE, SILVER ARSENOBENZOL, SILBER-SALVARSAN (*P.G. VI*), SILVER SALVARSAN (*Bayer Products, London*).

*Dose.*— $1\frac{1}{2}$  to 10 grains (0.1 to 0.6 g.) intravenously in 1% solution, one or two injections of 0.1 g. each, then 0.2 g for women, and 0.25 g. for men at intervals of not less than 4 days. Repeated at intervals until clinical symptoms and blood test satisfactory. In weakly patients begin with 0.05 g.

The sodium salt of silver 3 : 3'-diamino-4 : 4'-dihydroxyarsenobenzene. It is a brownish-black powder, containing 18 to 21% of As and 12 to 13% of Ag, readily soluble in water, with alkaline reaction. Ampoules contain 0.05, 0.1, 0.15, 0.2, 0.25 and 0.3 g.

Clinically 0.1 g. corresponds to about 0.2 g of arsphenamine or 0.3 g. of neoarsphenamine. It is thought to have the combined effect of arsphenamine and silver against syphilitic parasites. Mercury to be suspended during treatment. It is used especially for syphilis of the central nervous system, and must be given very slowly to avoid vasomotor disturbances.

**Contraindications.**—As for arsphenamine.

**MULTIPLE SCLEROSIS.** Silver arsphenamine the most effective remedy—0.05 g. twice weekly, increased to 0.15 or 0.2 g., the average total dose being 2.5 g.—*Brit med J. Epit*, 11/1924, 55; *J. trop. Med (Hyg)*, Apr, 1925, 168.

**LATE SYPHILIS.** Importance of thorough treatment in the first instance—to prevent late sequelæ. Sulfarsenol praised for use in myocarditis and aneurism. **TABES** Intravenous injections with deep subcutaneous injections. For intravenous use Silver Salvarsan and for subcutaneous Sulfarsenol G.P.I. Silver Salvarsan in large quantities—Col L. W. Harrison, *Lancet*, 1/1923, 4.

**TRICHINOSIS** Six to 10 intravenous injections of Silver Salvarsan make up the treatment usually required. Commencing with 0.05 g. the dose is increased with 0.05 g. each time until the dose of 0.30 g. is reached, then descended, decreasing the dose in the same proportion. The patients regained lost weight, abdominal pains ceased and cheeks again showed healthy colour—J. Ragany, *Med Rec*, N.Y., 1935, 142, 335.

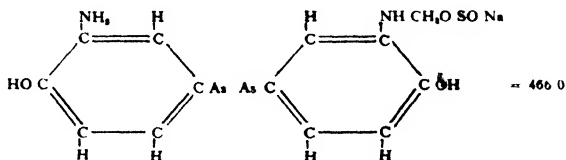
[P1 81] **Neoargentarsphenaminum** (*P. Helv V*) *Syn. and Prop. Name* NEOSILBERSALVARSAN (*P.G. VI*), NEOSILVER SALVARSAN (*Bayer Products, London*).

A molecular compound of neoarsphenamine and silver arsphenamine

[P1 81] **Neoarsphenamina** (*B.P., U.S.P. XI, F.E. VIII, P. Belg. IV, P. Helv V*). *Syn. and Prop. Names* "914," NOVARSENO BENZENE, NOVARSENO BENZOL, N.A.B., NEOARSENPHENOLAMINE, NEO-KHARSIVAN (*Burroughs Wellcome, London*), NEOSALVARSAN (*P.G. VI*) (*Bayer Products, London*), NOVARSENO BILLON (*Pharmaceutical Specialities (May & Baker) Ltd, London*), NOVARSAN (*Synthetic Drug Co., Toronto, Allen & Hanburys, London*), NOVOSTAB (*Boots, Nottingham*), ARSENO BENZOL ACID SODIUM FORMALDEHYDE-SULPHOXYLATE, SODIUM DIHYDROXYDIAMINO ARSENO BENZENE METHANESULPHONATE, NEOARSAMINOL (*P. Svec*). The proper name under the Therapeutic Substances Act is Neoarsphenamine.

*Dose*—2½ to 14 grains (0.15 to 0.9 g.) by intravenous injection. *U.S.P.* average dose—caution!—10 grains.

Consists mainly of sodium 3,3'-diamino-4,4'-dihydroxy-arsenobenzene-*N*-methylenesulphoxylate—



Neoarsphenamine is controlled by the Therapeutic Substances Act, 1925. It is made under licence and tested biologically (see Vol. II).

It is a yellow powder, readily soluble in water. The compound changes in the air, hence it is issued in sealed ampoules. The dry powder as taken from the sealed ampoules must contain not less than 18% or more than 21% of arsenic. *U.S.P. XI* requires 19 to 22%. The *B.P.* states that it contains approximately 20% of As. *Injections must be made immediately after preparation.*

**Manufacture.**—Aqueous solutions of arsphenamine and formaldehyde sulphonylate give a precipitate which is soluble in a minute quantity of alkali to form an almost neutral solution. The product differs according to temperature employed. At ordinary temperature the precipitate contains one "sulphur-acid" group.

**Uses.** Neoarsphenamine has almost entirely replaced arsphenamine owing to the ease with which solutions may be prepared—by simple solution in sterile water—and to the fact that it is less toxic. It is, however, also less toxic to spirochætes. Clinically it is found to have about two-thirds the activity of arsphenamine. It is given intravenously since intramuscular injections are painful, although the pain is reduced by using as solvent a solution of guaiacol 1, dextrose 50, sterile water to 100. For intramuscular injection sulpharsphenamine is more usual. Neoarsphenamine has been used in various diseases other than syphilis in place of arsphenamine.

**Dosage.**—Many authorities recommend an initial intravenous injection of a small dose, e.g., 0.45 g., followed by 8 to 10 doses at intervals of 3 to 8 days, gradually increasing the dose up to 0.75 or 0.9 g. as a maximum, repeating after an interval of 4 to 6 weeks. Three or four series may be required for complete treatment. Mercury or bismuth is frequently given during the intervals. 0.15 to 0.45 g. is given in from 5 to 10 ml. of water, or 0.6 to 0.9 g. in 15 to 20 ml. water, by slow injection into the median cephalic vein. More concentrated solutions have been employed, e.g., 0.9 g. in 2 to 3 ml. water, concentrated solutions, however, require great caution.

*For contraindications and treatment of after-effects see Arsphenamina.*

#### References.

**ANTHRAX** N.A.B., 0.6 g. intravenously daily, or on alternate days, is specific, will save life and render surgical intervention unnecessary. Treatment generally adopted throughout S. Africa.—A. B. M. Thomson (Durban), *Brit. med. J.*, 11/1931, 921.

Report of a case so treated with success at St. Olave's Hosp., Rotherhithe.—J. J. Coghlan and H. J. Shorvon, *ibid.* Widely used in this country.—C. G. Brentnall, *ibid.*, 966.

Nine patients with pustular anthrax were treated with neoarsphenamine only. Seven of them made remarkable recoveries, the other two, aged 1 year and 5 years, died. The results suggest that neoarsphenamine, if given within four days of the appearance of the pustule, will almost certainly cure the disease.—F. W. Gilbert, *Lancet*, 11/1935, 1283.

**BRONCHO-SPIROCHÆTOSIS** in China. Immediate relief; recovery after second or third administration.—E. C. Faust, *J. trop. Med. (Hyg.)*, Jan., 1923, 14.

**DISSEMINATED SCLEROSIS**, early cases treated with Novarsenobillon. Six weekly intravenous injections (0.15, 0.3, 0.45, 0.45, 0.6, 0.6 g.) repeated at end of six months, with arsenic *per os* in the interval.—W. Johnson, *Lancet*, 1/1923, 1209.

**GUINEA-WORM.**—Novarsenobillon 0.6 g. is the best treatment.—N. Cantlie, *J. trop. Med. (Hyg.)*, Feb. 1923, 39.

**HEMIPLEGIA** cured in three weeks by intravenous injections of 0.3 to 0.9 g.—L. Le Dentu, *J. trop. Med. (Hyg.)*, Oct., 1923, 312.

**HERPES ZOSTER.** Neoarsphenamine hypodermically causes disappearance of pain in 3 to 4 hours and disappearance of eruption in a few days. Second injection rarely necessary.—Milian, *J. Amer. med. Ass.*, 1/1929, 1024.

**LUNG AFFECTIONS, CHRONIC**, treated with intrapleural injection of Neosalvarsan. The pleura tolerates high dosage, 0.45 to 0.6 g. in 10 ml. water. It is a powerful antiseptic, especially against streptococci. It has been used in the bronchial tree in bronchiectasis.—*Lancet*, 11/1929, 32

**Spirochaetal pulmonary gangrene** well treated with neoarsphenamine intravenously.—B. S. Kline and S. S. Berger, *J. Amer. med. Ass.*, 11/1925, 1452

Intrathoracic injections valuable in suppurative lung conditions, e.g., gangrene, abscess, empyema and bronchiectasis. First aspirate pus and inject 0.15 g. Neosalvarsan, and repeat injection every 4 or 5 days, increasing to 0.6 g.—*Per Practitioner*, 11/1929, 155.

**MALARIA**. In early cases of simple tertian malaria an injection is of value.—*J. Amer. med. Ass.*, 11/1925, 151

Parasyphilitic affections of the nervous system treated by salvarsanised serum by means of double puncture. Small dose of Neosalvarsan added to patient's serum, and part re-injected.—T. Brunner, *Lancet*, 11/1929, 117.

**STAPHYLOCCAL INFECTIONS AND TRACHOMA**. Neoarsphenamine, 0.3 to 0.6 g. intravenously, is useful. Leucocytosis is powerfully stimulated.—G. R. S. Thomas, *Lancet*, 1/1925, 1292

**SYPHILIS**. *Sp. pallida* bathed in salvarsanised serum gradually lose their normal appearance, become ghostlike, fragmented and paralysed, and in about 5 days apparently die. Then in the space of 5 or 6 hours they recover their normal appearance and become as normal and active as control spirochaetes which have not been "doped." This suggests that arsphenamine should be injected at intervals of 5 days or less, instead of waiting the customary week, which gives the spirochaetes 3 days in which to recover. By attacking the spirochaetes when their vitality is at its lowest the largest number are killed in the minimum time, survivors and resistant forms are destroyed sooner, they are prevented from multiplying and are less likely to develop resistance to arsenic. On this foundation a bi-weekly course of injections was started at the White-chapel Clinic. The details are as follows—

**WHITECHAPEL COURSE**—*1st to 5th week*—Intravenous neoarsphenamine 0.45 g. weekly, bismuth 0.2 g., deep subcutaneous sulpharsphenamine 0.3 g. weekly, bismuth 0.2 g. *6th to 8th week*—Potassium iodide mixture 5 to 15 gr. thrice daily after meals. *9th to 13th week*—repeat as first 5 weeks. Patient to report for blood tests 7 days following last injection of course and again in 28 days, and then given potassium iodide mixture until next course begins. A prophylactic draught of concentrated liver extract and glucose is given before each injection. Three courses are given at intervals of 8 weeks. In patients over 45, or with late syphilis, a course of intravenous injections once a week only, or deep subcutaneous injections once a week only, spaced as above, may be given. This course was primarily prepared for those in the acute infectious stages, but the patient's age is important.

The effects of treatment on 241 consecutive cases gave 236 Wassermann-negative within a month after first course of treatment. There were comparatively few complications (5.8%) and these were mostly mild cases of dermatitis.—T. Anwyl-Davies, *Brit. med. J.*, 11/1933, 487. Confirmed by 10 years' experience at the Seaman's Hospital, Liverpool.—A. O. Ross, *ibid.*, 585. Also by E. T. Burke, *ibid.*, 623.

**Cardio-aortic syphilis** treated by, each year, a series of 6 to 8 intravenous injections of Novarsenobillon 0.6 g. at weekly intervals.—T. F. Cotton, *Brit. med. J.*, 1/1926, 855.

**SYPHILIS IN WOMEN**. Weekly intravenous injections of 0.3 to 0.6 g., with a drink of lemon-flavoured glucose solution (3 oz. each of glucose and water) half an hour before, and a Hutchinson's pill thrice daily. After a course of N.A.B. the pills are stopped for 2 weeks, and if the W.R. is negative and the case first seen in the primary stage, allow to carry on with pills alone for 2 months; but if case when first seen has well-established secondary lesions the patient is given pills to last a month and is then given a further set of injections, which may be slightly different from the first, e.g., Sulfarsenol instead of N.A.B. During remainder of treatment W.R. is taken every 3 months and a further course of injections

given if required. If all tests are negative and condition satisfactory, pills only are given during remainder of time. Standard of cure, negative W.R. over 2 years.—Margaret Rorke, *Modern Technique in Treatment*, Vol. I, p. 146.

**ANTE-NATAL TREATMENT OF CONGENITAL SYPHILIS.** The focus of infecting spirochætes is probably the placental tissue. Arsenical compounds and mercury at Glasgow given with 100% successes—J R C Greenlees, *Brit med J*, 11/1921, 654

Four or 5 intravenous injections of Neosalvarsan with mercurial inunctions during pregnancy. Results good—*Brit med. J.*, 11/1921, 654, 887.

**CONGENITAL SYPHILIS IN CHILDREN.** Vary dose according to age of child: *e g*, for child 1 month old, initial dose of N.A.B. 0.05 g., 1 to 3 years 0.1 g., and for older children 0.15 g., increasing during the course of six injections to respectively 0.1 g., 0.25 g., and 0.3 or 0.45 g., subsequent courses starting with larger doses and reaching higher maxima, but not exceeding 0.45 g for a child of 12. For older children commence with 0.04 to 0.06 g and increase up to 0.36 g. Injections are given intravenously or intramuscularly in from 1 to 3 ml distilled water. Mercury is given either as Hyd. c. Cret,  $\frac{1}{2}$  to 1 gr thrice daily, or better still, the ointment rubbed in once a day, or green iodide of mercury,  $\frac{1}{2}$  to  $\frac{1}{4}$  grain, 2 or 3 times daily during injections. In older children thirty or even forty arsenic injections may be necessary—D. Nabarro, *Modern Technique in Treatment*, Vol. III, p. 111

**INTRAPERITONEAL INJECTION** with safety in infants suffering from congenital syphilis. A child of 10 lbs should receive 50 mg., or 5 ml. of a solution consisting of 150 mg of neoarsphenamine dissolved in 15 ml. warm sterile water. The usual treatment consists of 4 injections at 3-day intervals, followed by 4 injections at 7-day intervals, the ideal site for entrance of the needle being in the middle of the left rectus sheath, slightly below the level of the umbilicus. The method is not so rapid as intravenous injections, but neoarsphenamine is absorbed with sufficient rapidity to act in any condition. It is ideal for children with small veins needing urgent treatment—H S Sanford, *J Amer med Ass*, 11/1925, 242

**TUBERCULOSIS** Organic compounds of arsenic, *e g*, "914" (intravenously) and Sulfarsenol (intramuscularly) in pulmonary tuberculosis where arsenic seems indicated—intramuscular route preferable. Improvement due to stimulation of the metabolic functions; there is no specific effect upon the bacilli—J Guy and G B Page, *Lancet*, 1/1924, 847

**YAWS**, acute, generally cured within 3 days by one injection of Novarsenobillon or Galyl—F. T. Auden, *Brit med J*, 11/1922, 83.

In Western Samoa, the standard treatment for yaws is three doses intravenously at 1-week intervals—Colonial Medical Report No 191, per *J trop Med. (Hyg.)*, Apr., 1926.

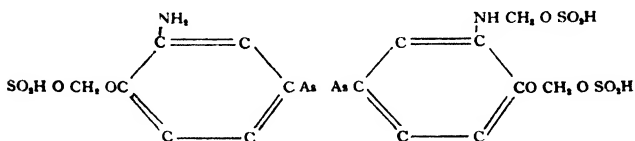
[P1-81] **Pigmentum Neoarsphenaminæ** (Mid H). *Syn* N A. B. PAINI  
Neoarsphenamine 5, glycerin 50, water to 100. For Vincent's angina

[P1-81] **Neoarsphenamine Suppositories** (0.10 g. in cocoa butter) given to three months' old baby with hereditary syphilis, with good results—E G Melon, per *J. trop med (Hyg.)*, Oct., 1922, 334.

[P1-81] **Sulpharsphenamina** (B.P., *P. Ital V*, *F.E VIII*, *P. Belg. IV*). *Syn. and Prop. Names* SULPHARSENOBENZENE, SULFARSENOL (*Laboratoire Biochimie Médicale, Paris*; *Modern Pharmacals, London*), KHARSULPHAN (*Burroughs Wellcome, London*), METARSENOBILLON (*Pharmaceutical Specialities (May & Baker) Ltd., London*), SULPHOSTAB (*Boots, Nottingham*), MYOSALVARSAN (*Bayer Products, London*), DI-SODIUM DIHYDROXY-

DIAMINOARSENOBENZENE-DIMETHYLENE SULPHONATE. The proper name under the Therapeutic Substances Act is Sulpharsphenamine

Described in the *B.P.* as consisting mainly of disodium 3 : 3'-diamino-4 : 4'-dihydroxyarsenobenzene-*N* · *N'*-dimethylene-bisulphite, but shown by Dyke and King to be a sodium salt of 3 : 3'-diamino-4 : 4'-dihydroxyarsenobenzene-*OO'*-*N*-trimethylenesulphurous acid—



Sulpharsphenamine is controlled by the Therapeutic Substances Act, 1925, and Therapeutic Substances Regulations, 1931. It must comply with tests for toxicity, therapeutic potency and stability. It is a yellow powder soluble in water, giving a faintly acid solution in which gelatinous particles must not be visible. It contains approx. 20% of arsenic.

**Dose**— $1\frac{1}{2}$  to 10 grains (0.1 to 0.6 g) by subcutaneous or intramuscular injection, in fairly concentrated solution. The following is suggested as a course in primary syphilis for an average adult:—

	Water		Water
1st day	0.12 to 0.18 g in 2 to 3 ml	19th day	0.54 to 0.6 g in 8 to 10 ml.
3rd "	0.18 " 0.3 g " 3 " 5 "	25th "	0.6 g " 10 "
5th "	0.30 " 0.42 g " 5 " 7 "	40th "	and later, Wassermann
8th "	0.42 " 0.6 g " 7 " 10 "	40th to 60th day,	Arrhenal
13th "	0.48 " 0.6 g " 8 " 10 "	61st day,	new series of injections

It is supplied commercially in a range of doses.

### **Toxic Effects and Contraindications.** As for Arsphenamina.

Dangers of sulpharsphenamine injections—*Brit med J Epit*, ii/1926, 92. Death following intravenous administration of sulpharsphenamine—J. R. Williams, *J Amer med Ass*, ii/1929, 1096.

**Uses.** It is less toxic than arsphenamine, and is used particularly for intramuscular injection because of freedom from pain. It is recommended for the treatment of congenital syphilis in infants, commencing with 0.05 g for an infant 1 to 2 months old. Mercury should also be given either as grey powder orally,  $\frac{1}{4}$  to  $\frac{1}{2}$  gr., or by inunction with mercury ointment. Sometimes given intravenously, but this is not advisable. It has given good results in other diseases such as gonorrhœa, arthritis, rheumatism, hyperkeratosis and epididymitis.

**GONORRHOEAL ARTHRITIS.** It is said to "act like a charm." **Dose.**—0.12 g. followed in 2 days by 0.18 g intravenously; three injections usually sufficient.—F. C. Doble, *Lancet*, i/1923, 1315.

**PUERPERAL SEPTICÆMIA** well treated subcutaneously, in doses of 0.12 g. In some cases 5 or 6 injections (at 1-day intervals) of 0.18 g were needed. Intravenously may be preferred in grave cases of septicæmia.—*Per J Amer med. Ass*, ii/1925, 393.

Good results with 0.06 g to 0.12 g. in puerperal fever.—*Lancet*, ii/1925, 28

**SYPHILIS.** Intramuscularly or subcutaneously in doses as high as 0.6 g. in 33% solution, without significant local reaction. End results favourable. Intramuscular injection the method of choice. Relatively high incidence of dermatitis, especially with intravenous injections. In congenital syphilis, as effective as neosarsphenamine.—*Per J. Amer. med. Ass.*, ii/1925, 1088.

[P1-81] **Bismarsen** (Abbott, Montreal; *Pharmaceutical Products, London*). Described as bismuth arspenamine sulphionate. It is a precipitation compound made by adding bismuth potassium tartrate to sulpharsphenamine and pouring the solution, made by means of soda, into methyl alcohol. A yellowish soluble compound with arsenic content 13% approx and bismuth content 24%.

Dose administered intramuscularly. Initial dose—0.1 g., followed by doses of 0.2 g. in 1 ml of sterile water, to which is added 2 minims Butyn 2% as local anæsthetic. Weekly doses at first, then 2 injections weekly for 20 injections. Repeat the course after an interval of a week. Children over 5 tolerate adult dosage well.

Of value in early syphilis. Toxicity low and reactions benign and controllable.—J. H. Stokes and S. O. Chambers, *J. Amer. med. Ass.*, ii/1927, 1500.

Criticism of the compound.—E. Tytler Burke, *Lancet*, i/1931, 1127.

Early syphilis treated with Bismarsen 0.1 to 0.2 g. intramuscularly.—Stokes, Miller and Beerman, *per Brit. med. J. Epit.*, i/1931, 110.

[P1-81] **Sulphoxyl-Salvarsan** (P.G. VI) (*Bayer Products, London*) is described as sodium *p*-arsenophenyl-dimethylaminopyrazolon-methylenesulphoxylate,  $C_{12}H_{10}O_4N_4As_2SNa$  = 774.2.

Dose.—8 to 12 ml intravenously at 2 to 3-weekly intervals. It is supplied only in isotonic solution containing 5% of the arsenic compound and 12% of lactose. Decomposition occurs on exposure of the solution to light and air.

Used in paralysis, frambæsia, syphilis and tertiary malaria.

[P1-81] **Mapharside** (Parke, Davis, London). Known as Mapharsen in U.S.A. *m*-Amino-*p*-hydroxyphenylarsine oxide, which is believed to be the compound formed in the body after injection of an arspenamine preparation. In dry ampoules containing 0.4 or 0.6 g. with sucrose and alkali.

Produced no toxic effects in dogs in amounts well above the therapeutic dose, and cleared up syphilitic lesions in rabbits in a dose of 1 mg. per kilo as well as did 10 mg. of Neosalvarsan, and caused disappearance of spirochætes from superficial lesions in a shorter time, it also had a greater effect on the Kahn reaction.—Gruhzit, *Arch. Derm. Syph.*, N.Y., Dec., 1935, 848.

Over a period of 18 months 233 persons were given 4666 intravenous injections of Mapharsen, the usual dose being 40 to 60 mg. (without addition of bismuth or mercury). Healing of visible lesions was rapid, comparing favourably with arspenamine. Wassermann reaction reversed to negative in nearly all cases of early syphilis, but in half of the cases there was serological relapse. Clinical relapse and return to positive serological findings occurred most frequently after irregular or short periods of therapy. Nitritoid reactions were not observed, but mild gastro-intestinal disturbances were not uncommon and Herzheimer reactions were occasionally noted. Mild jaundice occurred in four cases and increase of renal impairment in four others.—Foerster and co-workers, *Arch. Derm. Syph.*, N.Y., Dec., 1935, 868.

## ASAFŒTIDA

*B.P., U.S.P. XI, P. Helv. V*

Dose.—5 to 15 grains (0.3 to 1 g.). *U.S.P. XI* average dose 6 grains.

An oleo-gum-resin obtained by incision from the root of *Ferula fætida* or other species (*U.S.P. XI* from *F. Assa-fætida* and *F. fætida*). Occurs in greyish-white or yellowish tears, or in masses of agglutinated tears. Nervine stimulant, expectorant and carminative.

**Emulsum Asafœtidæ** (*U.S.P. XI*). Average dose.—½ ounce (15 ml.).

Asafœtida 1 in 25 of distilled water.

**Enema Asafetidae (B.P.C.).** *Dose.*—4 ounces (120 ml.). Tincture of asafetida 6 to 12% v/v in mucilage of starch. For intestinal flatulence.

**Mistura Asafetidae Composita (St T H)** Asafetida 5 gr., liquid extract of cascara sagrada 10 m., ammonium carbonate 4 gr., infusion of valerian to 1 oz.

**Pilulæ Asafetidae (B P C),** *dose*—1 or 2 pills, contain 3 grains. If required to be coated should first be coated with acacia mucilage and, when this is dry, with pill varnish. A silver coating may be applied over the varnish, which prevents the silver from being blackened.

**Spiritus Ammoniae Fetidus (B.P.C.).**

*Dose*—For a single administration, 1 to 1½ drachms (4 to 6 ml.), for repeated administration, 20 to 40 minims (1 2 to 2 5 ml.).

A distilled spirit representing 7½% w/v of asafetida with 10% v/v of strong solution of ammonia.

**Tinctura Asafetidae (B P).** 1 in 5. *Dose*—½ to 1 drachm (2 to 4 ml.)

**Liquor Antihystericus.** *Dose.*—½ to 1 drachm

On the Continent a mixture is used of camphorated spirit of ether and asafetida tincture equal parts

**Galbanum (B.P.C.)**

*Dose*—5 to 15 grains (0 3 to 1 g.).

Gum resin from *Ferula galbaniflua* (Umbelliferae) and other species. Expectorant and stimulant

**Pilulæ Galbani Compositæ (B.P.C.)** *Syn* PILULÆ ASAFETIDÆ COMPOSITÆ *Dose*—1 or 2 pills

Contain 1 grain each of galbanum, asafetida and myrrh.

**Myrrha (B.P., U.S.P. XI, P. Helv. V, P. Dan.).**

*Dose.*—5 to 15 grains (0·3 to 1 g.)

A yellowish or reddish oleo-gum-resin from *Commiphora molmol*, and possibly other species (Burseraceae). Soluble in water to the extent of about 50% (forms whitish emulsion on trituration), the remainder being mostly soluble in alcohol 90%. It is soluble in alkalis, e.g., potassium carbonate. A favourite constituent in mouth-washes, e.g., tincture of myrrh and borax.

**Tinctura Myrrhæ (B.P.).** *Dose.*—½ to 1 drachm (2 to 4 ml.). 1 in 5 of alcohol 90%.

**Tinctura Myrrhæ. (U.S.P. XI).** *Average dose*—30 minims (2 ml.) strength 1 in 5.

**Tinctura Myrrhæ Composita (B.P.C.)** *Syn* TINCTURA MYRRHÆ ET ALOES Myrrh and aloes of each 5% w/v in diluted alcohol

**Tinctura Myrrhæ et Boracis (B.P.C.)** Contains about 33% v/v of tincture of myrrh with tincture of krameria, borax and aromatic oils. Used as an astringent mouth-wash and gargle

**Sagapenum.**

*Dose*—10 to 30 grains (0 6 to 2 g.). A gum-resin, obtained from a species of *Ferula*, with taste resembling that of asafetida, and properties similar to this and galbanum. Has been given in amenorrhœa and hysteria

## ATROPINA

*B.P., Fr. Cx., U.S.P. XI, F.E. VIII.*

$C_{17}H_{23}NO_3 = 289\cdot19.$

[P1] "Alkaloids, the following; their salts, simple or complex:—*Atropine.*"



[81] "*Alkaloids, the following; their salts, simple or complex.—Atropine except substances containing less than 0.15 % of atropine.*"

**Dose.**— $\frac{1}{15}$  to  $\frac{1}{80}$  grain (0.00025 to 0.001 g.). The dose may be increased to  $\frac{1}{8}$ , or in acute mania to  $\frac{1}{4}$  grain or more. *Fr. Cx*—*Maximum dose* in 24 hours  $\frac{1}{4}$  grain approx. It is generally given internally as the sulphate

An alkaloid obtained from *Atropa Belladonna*, and other solanaceous plants. Generally in acicular crystals, alkaline in reaction; m p. 114° to 116°.

**Soluble** 1 in 560 of water, 1 in 3 of 90% alcohol, 1 in 16 of ether (*Fr. Cx.* 1 in 25), 1 in 1 of chloroform, 1 in 40 of olive oil, freely soluble in glycerin and oleic acid

**Incompatible** with caustic alkalis and mercurial salts. Alkalis cause hydrolysis into tropine and alkali tropate. The change takes place when solutions are left in contact with ammonia or alkali carbonates and to some extent with bicarbonates

The mydriatic alkaloids, atropine and hyoscyamine, may be manufactured from *Atropa Belladonna*, *Datura Stramonium*, *Duboisia myoporoides* and *Hyoscyamus niger*, and hyoscine may be obtained from the last two plants. Atropine is *dl*-hyoscyamine. It does not exist as such in these plants, but is produced from the *l*-hyoscyamine by careful racemisation with alkali

**Antidotes.** Give 20 gr. of tannic acid in 4 oz. of water, then empty the stomach by emetic (which may not be effectual) or by a stomach tube (which should be well lubricated because of the dryness of the mucous membrane), using dilute tannic acid solution or a solution of potassium permanganate 60 gr. in 2 gallons of water. Medicinal charcoal, 2 dr in 4 oz. of water, may be administered. Keep the patient warm. Give fluids freely to aid excretion. Hot, strong coffee may be given by rectum. Oxygen inhalations and artificial respiration may be necessary. Morphine and pilocarpine are not recommended.

**Uses.** Atropine and its salts are used for ophthalmic purposes to dilate the pupil and paralyse accommodation.

Given internally or hypodermically, they are antagonistic to opium and morphine, calabar bean and physostigmine, jaborandi and pilocarpine, aconite and aconitine, and hydrocyanic acid. Physiologically, whilst atropine acts as a stimulant to the motor area of the central nervous system, it paralyses the terminations of peripheral parasympathetic nerves, and those supplying glands and heart. It is used to lessen secretions, especially the saliva, bronchial secretion and gastric juice. It lessens the perspiration, especially the night sweats of phthisis. It has no effect on the amount of the urine

Small doses reduce peristalsis, and are added to purgatives to prevent griping.

It is also injected intramuscularly in doses of at least  $\frac{1}{80}$  gr to relieve pain in sciatica and muscular rheumatism, and is given to check bed wetting, and to relieve spasm of pain of urinary calculus,

cystitis and prostatitis. Relieves bronchial spasm, whooping cough and asthma.

Colds can be aborted by a dose of  $\frac{1}{16}$  to  $\frac{1}{8}$  grain (sulphate), dissolved in a tumbler of water and the whole sipped in the course of an hour; it is repeated next day if necessary;  $\frac{1}{2}$  minim of *Liquor Atropinæ Sulphatis* per day for 10 days is often of value as a preventive of recurrent colds

Injections of atropine, usually combined with strychnine, are useful in the treatment of inebriety.

Hypodermically prior to chloroform or ether, it is of value as an antidote to the cardio-inhibitory effects of the anæsthetic, and to reduce bronchial secretion due to the irritant effect, particularly of ether

Full doses are of value in pulmonary and other forms of hæmorrhage. The dose must be pushed until toxic symptoms, such as dry mouth and dilated pupils, are developed; as much as  $\frac{1}{16}$  gr. may be given every 2 to 4 hours. The action of atropine on the heart is, in general, antagonistic to that of digitalis. It is of value in partial heart-block not due to organic causes, but is contra-indicated in complete block. In acute cardiac failure, especially if there is pulmonary œdema, very large doses (up to  $\frac{1}{16}$  gr. or more hypodermically) may be of service

It is largely used in ophthalmology as a mydriatic and to paralyse accommodation. Its effect may last for several days, and it has the disadvantage of increasing intraocular tension and may therefore increase a tendency to glaucoma

#### References to Use of Atropine and its Salts.

**GASTRIC ULCER.** For diminishing the secretion of acid in gastric ulcer give  $\frac{1}{32}$  gr of atropine sulphate in 1 dr of water before three of the feeds and a double dose the last thing at night. Increase both doses by 10 minims ( $\frac{1}{16}$  gr of atropine sulphate) every day until the patient complains of dryness of the mouth or paralysis of accommodation. Reduce the doses by 10 minims and continue throughout the period of treatment. The influence of atropine on salivary secretion is approximately parallel to its influence on gastric secretion. It is impossible to guess what will be the adequate dose in an individual—A F Hurst, *Pharm. J.*, 11/1934, 703

In single maximum doses by hypodermic injection, atropine may have a limited value in reducing secretion and spasm, but in the doses usually employed by mouth, or permissible for any continued treatment, atropine and belladonna are practically without effect on the secretory and motor functions of the stomach—W A Bastedo, *J Amer med Ass.*, 1/1936, 88

In stomach disorders, atropine,  $\frac{1}{16}$  to  $\frac{1}{8}$  gr., in 1 ml of saline solution *intravenously* gives relief from nausea, vomiting and pain within from 2 to 5 minutes in patients with smooth muscle spasm secondary to a peptic ulcer or pylorospasm, and in other symptoms thought to be related to the parasympathetic nervous system, including angina pectoris, biliary dyskinesia, ulcerative colitis and the dyspnoea of asthma—E. A. Lehnher, *J. Amer med Ass.*, 1/1936, 642.

**INFANTS** may receive atropine in alcoholic solution, e.g., 0.1 mg (max initial dose), most infants bear it well. It often has a tranquillising effect in excessively nervous children and may arrest habitual vomiting and pylorospasm; eczema and exudative diathesis is sometimes influenced favourably. Best given before meals—Per *J. Amer med. Ass.*, 11/1925, 938. It may cause severe reaction with hyperpyrexia and abdominal distension. Fever reduced by hydrotherapy. No harmful after-effects. Dose should be increased slowly—G. F. Munns, *ibid.*, 11/1929, 171.

**HEART BLOCK.** Small doses of atropine slow the heart, whereas large doses cause acceleration. Small doses increase heart block, but large doses tend to

remove it. Individuals vary considerably in reaction, but  $\frac{1}{160}$  gr., as a rule, slows the heart — *Brit. med J. Ept.*, i/1925, 11.

**INEBRIETY.** On commencing treatment give a general tonic and stomachic to reduce physical craving for alcohol, *e.g.*, the following mixture 6 times daily. Atropine sulphate solution  $\frac{1}{2}$  m., strychnine hydrochloride solution 1 m., compound tincture of cinchona  $\frac{1}{2}$  dr., glycerin  $\frac{1}{2}$  dr., compound infusion of gentian to  $\frac{1}{2}$  oz. After 4 days this is replaced by the following every 2 hours. Liquid extract of cascara 10 m., compound tincture of cinchona  $\frac{1}{2}$  dr., aloin  $\frac{1}{8}$  gr., strychnine hydrochloride solution 3 m., and compound infusion of gentian to 1 dr. The strychnine is omitted after 1 week. Colloidal gold (2 ml daily) is also given in equal doses thrice daily, after meals, continued for 3 weeks — P. Bonsfield, *Lancet*, ii/1925, 1150.

**LABOUR.** Atropine appears to stimulate contractions. It certainly has no inhibitory action. — A. W. Bourne and J. H. Burn, *Brit. med J.*, ii/1930, 87.

**MIGRAINE** well treated by Liquor Atropinæ Sulphatis 1 to 3 minims 3 times daily after meals — H. D. O'Sullivan, *Brit. med J.*, i/1923, 18.

**POST-ENCEPHALITIC PARKINSONISM.** Treatment of 16 cases with a dosage of 3 to 5 minims three times a day of a 0.1% solution of atropine sulphate, the dose being increased every day, every other day, or every third day by 1 minim until a single dose contains over 1 mg., when it is given in pill form until an optimum effect is obtained — usually at a dosage of 4 to 8 mg. 3 times a day. Rigidity banished in 6 and diminished in 7 cases, tremor (in 9 cases) disappeared in 1 and diminished in 7. But atropine alone is inadequate, it must be supplemented by such measures as salt-water baths, massage, gymnastics, courses of arsenic and psychic encouragement — O. J. Nielsen, *Hospitalstidende*, 1935, 806.

**PREMEDICATION IN ANÆSTHESIA.** Morphine better than atropine as a premedicant. Atropine has actually a stimulant effect and may facilitate onset of shock instead of delaying it — R. J. Clausen, *Brit. med J.*, ii/1931, 377.

Atropine is the most valuable premedicament of all, and should be used before all anæsthetic agents and in all cases except where the basal metabolic rate is high. It inhibits the action of the vagus and diminishes mucus secretion. It should be given hypodermically, in doses of  $\frac{1}{160}$  to  $\frac{1}{80}$  grain, 1 hour before operation, except in the case of children, when it is better to give tincture of belladonna by the mouth — F. W. Green, *Brit. med. J.*, ii/1935, 781.

**PYLORIC STENOSIS.** Begin with small dose of 3 or 4 drops of 1 in 1000 watery solution of atropine sulphate half an hour before feed, increased till child is receiving 35 to 45 drops in 7 or 9 drop doses 5 times daily. Results best perceived when given over a period of weeks — J. L. Meagher, *Brit. med J.*, i/1926, 89.

**SEASICKNESS.** As preventive,  $\frac{1}{80}$  gr. atropine sulphate *per os*, followed by 2 doses of  $\frac{1}{160}$  gr. at  $\frac{1}{2}$ -hour intervals. Also given for treatment — *Brit. med J. Ept.*, ii/1928, 75.

Tolerance to atropine can be developed by most people if the drug is given in gradually increasing doses. Thus, before long voyages, patients susceptible to seasickness are given atropine as follows: 4 days before embarking 1 mg. is given in 4 doses; the dose is increased by 1 mg. a day so that 4 mg. is taken during the day of departure, and this dosage is maintained throughout the voyage. In patients with pyloric ulcer, a dose as high as 19 mg. a day has been reached — Danielopolou and Radulesco, per *Lancet*, i/1936, 909.

#### ATROPINE AND STRYCHNINE INJECTION TREATMENT FOR INEBRIETY —

First week, Atropine  $\frac{1}{160}$  grain, with Strychnine  $\frac{1}{80}$  grain t. i. d.

Second " "  $\frac{1}{80}$  " " " "  $\frac{1}{40}$  " " "

Third " "  $\frac{1}{40}$  " " " "  $\frac{1}{20}$  " " "

Fourth " "  $\frac{1}{20}$  " " sine Strychnina

together with a mixture of extract of cinchona, sal volatile, and spirit of chloroform thrice daily. A little capsicum may also be added.

#### [P. 81] Chloroformum Atropinæ (B.P.C.)

1 in 220 in chloroform coloured with alkanna. A rubefacient and anodyne application in neuralgia and rheumatism. Cleaner in use than Chloroformum Belladonnæ.

#### [P. 81] Collodium Atropinæ (B.P.C.).

1 in 220 in acetone and acetone collodion. A colourless substitute for belladonna plaster. Allays the irritation of chilblains.

[P1 81] **Unguentum Atropinæ** (B.P.C.). 1% in white soft paraffin.

[P1 81] **Atropinæ Sulphas** (B.P., P.G. VI, P. Dan, P. Helv. V, P. Jap., U.S.P. XI, F.E. VIII, P. Belg IV, P. Ital V).  $(C_{17}H_{23}O_3N)_2 \cdot H_2SO_4 \cdot H_2O = 694.5$ . P. Ned V has  $2H_2O$ .

*Dose*.— $\frac{1}{160}$  to  $\frac{1}{80}$  grain (0.00025 to 0.001 g). The dose may be increased to  $\frac{1}{40}$ , or in cases of acute mania  $\frac{1}{2}$  grain. P. Dan. gives  $\frac{1}{80}$  to  $\frac{1}{40}$  grain U.S.P. XI average dose  $\frac{1}{160}$  grain Fr Cx. has maximum dose in 24 hours  $\frac{1}{32}$  grain approx., P.G. VI  $\frac{1}{4}$  grain, P. Belg.  $\frac{1}{80}$  grain

Opaque white minute efflorescent crystals or granules

**Soluble** 1 in less than 1 of water, 1 in 4 of alcohol 90%.

**Incompatibles.** Bromides, iodides Quinine hydrochloride is incompatible, but the acid hydrochloride does not precipitate in reasonable dilutions See also under Atropina.

Atropine sulphate in simple aqueous solution (pH 6.54) may be sterilised at 120° for 20 minutes, but if the reaction is made faintly alkaline (pH 7.3) more than 50% is decomposed by this treatment Homatropine hydrobromide solutions must not be heated—S A Schou and P B Bjerregaard, *Dansk. Tidsskr Farm.*, 1932, 10, 185

[P1 81] **Glycerinum Atropinæ** (B.P.C., St T H.)

Atropine sulphate, 1 in 400, with compound tincture of lavender and glycerin This is more cleanly than Glycerinum Belladonnæ and does not stain UCH is similar.

The resinous matter in the compound tincture of lavender deposits The following keeps better Atropine sulphate 127½ gr, water 25 oz, spirit of lavender 2 m, spirit of rosemary 2 m., cinnamon oil 1 m., magenta solution q s., alcohol 90% 1 oz, glycerin to 100 oz

[P1 81] **Granules de Sulphate d'Atropine** (Fr Cx) contain 1 mg

[P1 81] **Guttæ Atropinæ** (R.L.O.H.) Atropine sulphate 1, 2, 4 or 8 gr., sterilised water to 1 oz

St T H has 0.5, 1 or 2%, UCH and St MH 0.5 or 1%, WH 1%

[P1 81] **Gutt. Atropin. Dil.** (N I F)

Atropine sulphate  $\frac{1}{4}$  gr., distilled water to 2 dr

Poisoning in a child of five following instillation into each eye of 2 drops of a 1% solution of atropine sulphate There was restlessness, singing and shouting, and finally convulsions, a scarlatiniform rash developed, with dryness of mouth and dilatation of pupils Recovery following morphine injections Review of literature—C M Scally, *Brit med J*, 1/1936, 311

[D P1 81] **Guttæ Atropinæ et Cocainæ** (St T H)

Atropine sulphate 2% and cocaine hydrochloride 2% in sterilised water

[P1 81] **Guttæ Atropinæ et Quininæ** (Liverpool Eye and Ear Infirmary)

Atropine sulphate 4 gr., quinine sulphate (bisulphate) 4 gr., distilled water 1 oz.

[P1 81] **Hypodermic Tablets** contain  $\frac{1}{320}$ ,  $\frac{1}{160}$ ,  $\frac{1}{80}$ ,  $\frac{1}{40}$ , and  $\frac{1}{20}$  gr. in each, also [D P1 81]  $\frac{1}{160}$  gr combined with morphine sulphate  $\frac{1}{4}$  gr., and atropine sulphate  $\frac{1}{320}$  gr combined with morphine sulphate  $\frac{1}{4}$  gr., vide also morphine sulphate

[P1 81] **Lamella Atropinæ** (B P)

Contain  $\frac{1}{80000}$  grain (0.000013 g.) of the sulphate in each, for dilating the pupil; others containing [P1 81]  $\frac{1}{8000}$  gr. (R.L.O.H.) paralyse the accommodation Also prepared containing [D P1 81] atropine sulphate  $\frac{1}{10000}$  gr. combined with cocaine hydrochloride  $\frac{1}{4000}$  gr. and [D P1 81] cocaine  $\frac{1}{800}$  gr. with atropine  $\frac{1}{8000}$  gr. R.L.O.H. has [D P1 81] atropine  $\frac{1}{800}$  gr., cocaine  $\frac{1}{800}$  gr.

**[P1-81] Linimentum Atropinæ.**

Atropine 1 (more or less, if ordered), oleic acid 15, castor oil 15, oil of lavender 1, alcohol (90%) *q s* to 100

In lumbago and other rheumatic affections is very serviceable used with gentle friction; it is readily absorbed

**[P1 81] Linimentum Atropinæ (St. T H)**

Atropine sulphate 38½ gr, compound tincture of lavender 100 m, industrial methylated spirit to 20 oz A non-staining preparation of the same strength as Lin. Belladonnæ

**[P1 81] Linimentum Atropinæ et Chloroformi (St T H)**

Liniment of atropine (St T H) 5, chloroform 1

**[P1 81] Liquor Atropinæ Sulphatis (B P C).**

*Dose.*—½ to 1 minim (0.03 to 0.06 ml), or more

Strength 1% *w/v* Should be freshly prepared

**[P1] Mistura Antidipsomania.**

*Dose*—½ ounce (15 ml)

Concentrated liquors of commerce of cinchona and gentian 10 m, of capsicum ½ m, solution of strychnine nitrate (4 gr to the oz) 1 m, of atropine sulphate (1 gr to the oz) 1 m, glycerin 1 dr, water to ½ oz Has been found of great value with the strychnine and atropine injections, gradually diminished in strength

**[P1 81] Oculentum Atropinæ (B P) 0.25% of atropine sulphate in simple eye ointment.**

**[P1 81] Unguentum Atropinæ (R L O H)** Atropine 2, 4 or 8 gr, yellow soft paraffin to 1 oz Dissolve atropine in chloroform and add to soft paraffin heated to 61°

**[P1] Oculentum Atropinæ cum Hydrargyri Oxido (B P.).**

0.125% of atropine sulphate and 1% of yellow mercuric oxide in simple eye ointment.

**[P1 81] Unguentum Hydrargyri Oxidi Flavi cum Atropina (R L O H)**

Atropine 2 or 4 gr, freshly precipitated yellow mercuric oxide 4 gr, yellow soft paraffin to 1 oz Dissolve the atropine in chloroform, mix with the yellow soft paraffin heated to 61° and add the mercuric oxide while cooling

CORNEAL ULCERS are well treated with an ointment containing atropine and yellow mercuric oxide of each 1% —P G Doyne, *Lancet*, 11/19/27, 132

**[D P1 81] Oculentum Atropinæ et Cocainæ (B P C.). 0.25% of atropine sulphate and 0.5% of cocaine hydrochloride in simple eye ointment**

**[D P1 81] Unguentum Atropinæ et Cocainæ (R L O H)** Atropine 4 gr, cocaine 8 gr., yellow soft paraffin to 1 oz Proceed as under Unguentum Atropinæ (R.L.O.H.)

**[P1] Oculentum Iodoformi et Atropinæ (B P.C).**

5% of iodoform and 0.1% of atropine sulphate in simple eye ointment.

**[P1-81] Unguentum Iodoformi cum Atropina (R L O H).**

Atropine 2 gr., iodoform 60 gr, yellow soft paraffin to 1 oz Prepare as Ung Hyd. Ox. Flav. c. Atropin. (R L O H)

**[P1 81] Oleum Atropinæ.**

Atropine 1, castor oil *q s* to 100 Heat to dissolve (R L O H 4 grains in 1 ounce). Forms a stable solution

**[P1] Pessaries of Atropine** are prepared (weight 120 grains) with gelatin mass or at times with oil of theobroma, containing generally ⅔ gr of the alkaloid in each.

**[P1 81] Pilula Atropinæ, ⅔ gr, 1½ gr, 1 gr, ⅔ gr, ⅔ gr grain in each**

Taken at night, to check sweating. May cause dryness of the throat

**[P1 81] Pilula Atropinæ ⅔ gr, Arsenici ⅔ gr, grain, et Quininæ 1½ grains**  
Quinine sulphate 150 gr., arsenious acid trituration 10 gr, atropine sulphate trituration 5 gr, with lactose and powdered acacia *q s* to make 100 pills. For catarrhal cold, if taken in early stage, 1 every 3, 4, or 6 hours, "nips it in the bud."

[P1] **Antidypso** (*Hewlett, London*) A tonic combining the "atropine and strychnine" treatment of alcoholism. Contains 1 m of 1% strychnine nitrate solution and 1 m of 0.25% atropine sulphate solution per dr

**Compound Asthma Fluid** (*Martindale, London*)

It contains, among other ingredients, a small proportion of atropine, and is found of considerable value in preventing attacks of asthma. It is prepared in three strengths, [P1] "A," 0.6 gr. atropine sulphate per fl oz, [P1 81] "B" 1.2 gr, [P1 81] "C" 2.4 gr

[P1 81] **Atropinæ Methylbromidum.** *Syn* MYDRIASINE.

$C_{17}H_{23}O_3N, CH_3Br = 384.1$ .

*Dose* —  $\frac{1}{80}$  to  $\frac{1}{40}$  grain (0.001 to 0.002 g.)

An addition product of methyl bromide to the alkaloidal base

White crystals soluble in water 1 in 1 easily M p about 222°

**Uses.** Internally similar to those of atropine. Subcutaneously in croupous pneumonia, dry pleurisy and appendicitis, dyspepsia with pyrosis (with sodium bicarbonate), and epilepsy (with bromide) As effect passes off rapidly it is useful in  $\frac{1}{2}$  to 2% solution with cocaine hydrochloride 1% for dilating the pupil in suspected iritis to ascertain whether adhesions exist.

[P1 81] **Atropinæ Methylnitrates.** *Prop Name* EUMYDRIN (*Bayer Products, London*)  $C_{17}H_{23}O_3N, CH_3NO_3 = 366.2$ .

*Dose.* —  $\frac{1}{80}$  to  $\frac{1}{40}$  grain (0.001 to 0.002 g.)

White crystals, soluble in water, obtained by the action of silver nitrate on atropine methylbromide.

A powerful mydriatic, and less poisonous than atropine. 1 or 2% solution dilates the pupil after 25 minutes; the maximum is reached in 50 minutes. Dilatation persists for 12 hours. Also given internally in congenital pyloric stenosis

[P1 81] **Guttæ Methylis Atropinæ Nitratis** (*R L O H*) *Syn* GUTTÆ EUMYDRINÆ Atropine methylnitrate 2 or 4 gr, sterilised water to 1 oz

**CONGENITAL PYLORIC STENOSIS** Eumydrin gives better results than surgery, gastric lavage, or atropine. It is given in the form of a 1 in 10,000 solution (solution does not keep) which is given in a dosage of 5 ml ( = 0.5 mg per dose) 7 times a day half an hour before feeding, in many cases doses of 0.25 mg may prove sufficient. The treatment is continued until the patient has not vomited for a week or more. It is important not to give this treatment as long as the patient is in an extremely dehydrated condition, and not until the introduction of saline has produced satisfactory diuresis. From 1911 to 1922 in the Children's Department of the Rigshospital, Copenhagen, congenital pyloric stenosis was treated by gastric lavage and feeding through a duodenal tube. From 1922 to 1927 atropine was given, and since 1927, Eumydrin. During these periods respectively, 71, 47 and 61 patients were treated. The following summarises the results in these three groups of patients: the average number of days spent in the hospital were 103, 96 and 77, and the mortality 7.1%, 6.4% and 1.6%. The average initial loss of weight was 0.263 kg, 0.230 kg and 0.089 kg. Average weight upon discharge was 3.995, 4.540 and 4.605 kg. The average increase in weight per week was 62, 91 and 122 g — *E. Svensgaard, Arch. Dis. Childh*, 1935, 443

[P1 81] **Atropinæ Salicylas.**  $C_{17}H_{23}NO_3, C_7H_6O_3 = 427.2$ .

*Dose.* —  $\frac{1}{80}$  grain (0.001 g.).

Deliquescent powder or crystals, stated to be superior to the sulphate as more rapid in effect. Soluble 1 in 20 of water.

[P1] **Liquor Atropinæ Salicylatis.** Atropine  $\frac{1}{2}$  gr., salicylic acid  $\frac{1}{2}$  gr., water 1 oz.

**Homatropina.**  $C_{16}H_{21}NO_3 = 275.2$ 

[P1] "*Alkaloids, the following; their salts, simple or complex:—Homatropine.*"

[S1] "*Alkaloids, the following; their salts, simple or complex.—Homatropine except substances containing less than 0.15% of homatropine.*"

Dose —  $\frac{1}{64}$  to  $\frac{1}{32}$  grain (0.001 to 0.002 g.)

Homatropine is the mandelic acid ester of tropine. In colourless crystals, insoluble in water, soluble in organic solvents and 1 in 100 of liquid paraffin; also soluble in vegetable oils.

**Uses.** Preferred to atropine as a mydriatic for examining the eye, because its action is more rapid and less prolonged. The effect is exerted in 15 to 30 minutes, and passes off in 6 to 24 hours. Mydriasis is readily controlled by physostigmine. Homatropine is rarely used internally. Large doses may cause, like atropine, staggering gait, and delirium in children. Homatropine slows the heart beats and renders them irregular in force and rhythm.

[P1 S1] **Oleum Homatropinæ (R L O H)**

Homatropine 4 gr., dissolved in minimum quantity of chloroform and mixed with castor oil at 61° to 1 oz., stir until cold.

[D P1 S1] **Oleum Homatropinæ et Cocainæ (R L O H)** contains 8 gr. of homatropine and 8 gr. of cocaine per oz. of castor oil. Prepared as the preceding. These oily solutions are not washed out by the tears.

The preparation of a solution in castor oil without the chloroform necessitates warming the alkaloid and oil on a water-bath for several hours.

[P1 S1] **Homatropinæ Hydrobromidum (B P, U.S.P. XI, P.G. VI, P. Dan., P. Helv. V, P. Svec., P. Jap., P. Belg. IV, P. Ital. V, F.E. VIII)**  $C_{16}H_{21}O_3N.HBr = 356.10$

Dose.— $\frac{1}{64}$  to  $\frac{1}{32}$  grain (0.001 to 0.002 g.) U.S.P. XI average dose  $\frac{1}{128}$  grain.

In minute trimetric crystals; m.p. about 214° (decomp.).

**Soluble** 1 in 6 of water, 1 in 18 of alcohol 90%, and 1 in 1.33 of dehydrated alcohol; slightly soluble in ether, insoluble in chloroform.

[P1-S1] **Lamellæ Homatropinæ (B.P.)** contain  $\frac{1}{160}$  gr. (0.0006 g.) of homatropine hydrobromide.

[P1 S1] **Guttæ Homatropinæ (R L O H)** 4 or 8 gr. of homatropine hydrobromide per oz. of sterile water.

[D-P1-S1] **Guttæ Homatropinæ et Cocainæ (R.L.O.H.)**. Homatropine hydrobromide 4 or 8 gr., cocaine hydrochloride 8 gr., sterilised water to 1 oz.

[P1-S1] **Injectio Homatropinæ Hypodermica**, 1 in 120, is used.

Dose.—1 to 6 minims (0.06 to 0.4 ml.).

**Euphthalmin (Schering, London).** Hydrochloride of phenylglycolyl-N-methylvinylidiacetonalkamine. Used in a 5 or 10% solution as a mydriatic.

[P1-S1] **Syntropan (Hoffmann-La Roche, London)** 3-Diethyl-amino-2,2-dimethylpropanol ester of tropic acid. A synthetic antispasmodic. Dose—1 tablet (0.05 g.) 3 or 4 times a day; or by injection 1 ml. (= 0.01 g.) 3 times a day. In all vagotonic states, e.g., vascular tension, coronary spasm, angina pectoris, gastric spasms, dysmenorrhœa.

**SEA-SICKNESS** Tried out with success in twelve cases during a ten weeks voyage to S. America; it gave immediate relief.—Thos. North, *Lancet*, i/1936, 1263.

## AURANTIUM

(with notes on LEMON and ASCORBIC ACID)

### **Aurantii Cortex Recens (B.P.) and Aurantii Cortex Siccatus (B.P.).**

The fresh or dried outer part of the pericarp of the ripe or nearly ripe bitter-orange, the fruit of *Citrus Aurantium*

*U.S.P. XI* includes dried bitter-orange peel and fresh sweet-orange peel

#### **Elixir Simplex (B.P.C.).**

*Dose.*—1 to 2 drachms (4 to 8 ml).

Tincture of orange about 1 in 13 with syrup and distilled water.

#### **Extractum Aurantii Liquidum (B.P.C.)**

*Dose*—10 to 20 minims (0.6 to 1.2 ml) About 1 in 1, from dried bitter-orange peel

#### **Infusum Aurantii Compositum Concentratum (B.P.C.)**

*Dose*— $\frac{1}{2}$  to 1 drachm (2 to 4 ml)

Dried bitter-orange peel, 1 in 5, with lemon peel and clove. It is approximately eight times the strength of the fresh infusion

#### **Infusum Aurantii Compositum Recens (B.P.C.)**

*Dose*— $\frac{1}{2}$  to 1 ounce (15 to 30 ml)

Dried bitter-orange peel, 1 in 40, with lemon peel and clove.

#### **Infusum Aurantii Concentratum (B.P.)**

*Dose.*— $\frac{1}{2}$  to 1 drachm (2 to 4 ml) About 1 in 2 $\frac{1}{2}$ . It is approximately eight times the strength of the fresh infusion

#### **Infusum Aurantii Recens (B.P.).**

*Dose*— $\frac{1}{2}$  to 1 ounce (15 to 30 ml) 1 in 20

#### **Syrupus Aromaticus (B.P.C.).**

*Dose.*— $\frac{1}{2}$  to 1 drachm (2 to 4 ml)

Liquid extract of orange peel, 1 in 16, with cinnamon water and syrup

#### **Syrupus Aurantii (B.P.).**

*Dose*— $\frac{1}{2}$  to 2 drachms (2 to 8 ml).

Tincture of orange 1, syrup 7.

#### **Syrupus Aurantii (U.S.P. XI)**

Tincture of sweet-orange peel 5, citric acid 0.5, talc 1.5, mixed with water sufficient after filtering to give 45, dissolving sucrose 82 in the filtrate in the cold, and adding water to produce 100

#### **Tinctura Aurantii (B.P.).**

*Dose*— $\frac{1}{2}$  to 1 drachm (2 to 4 ml)

1 of fresh bitter-orange peel in 4 of alcohol 90% Mixtures containing salts of iron will become dark in colour with all preparations of orange peel.

#### **Tinctura Aurantii Amari (U.S.P. XI)**

*Average dose.*—60 minims (4 ml)

Dried bitter-orange peel in 60% alcohol, 1 in 5

#### **Tinctura Aurantii Dulcis (U.S.P. XI).**

*Average dose.*—60 minims (4 ml)

Fresh outer rind grated from sweet-orange peel, in alcohol, 1 in 2.



**Vinum Aurantii (B.P.C.)**

Made by fermentation of a saccharine solution containing fresh bitter-orange peel. It contains 12 to 16% *v/v* of ethyl alcohol. In practice a boiling 25% sugar solution is poured on to the peel and allowed to stand for 24 hours. Yeast is added and the liquor fermented at 20° for 3 days.

**Oleum Aurantii (B.P.C.)** *Syn.* ESSENCE OF ORANGE

*Dose* — $\frac{1}{2}$  to 3 minims (0.03 to 0.2 ml).

Is obtained either from the sweet-orange or from the bitter-orange, chiefly from the former. The two oils are practically indistinguishable chemically. On keeping, a disagreeable terebinthinate taste develops, stated to be prevented by the addition of 10% of dehydrated alcohol to the freshly distilled oil.

**Terpeneless Oil of Orange** is prepared, being many times (about 65) more potent in flavour and soluble in 60% spirit.

**Elixir Aromaticum (B.P.C.)** *Syn.* ELIXIR AURANTII, ELIXIR AURANTII COMPOSITUM.

*Dose.*— $\frac{1}{2}$  to 2 drachms (2 to 8 ml.)

Contains oils of orange, coriander and anise, in alcohol, syrup and water.

**Elixir Aromaticum (U.S.P. XI)**

Compound spirit of orange 1.2%, with syrup, alcohol and water, and clarified by filtration with 3% of talc.

**Elixir Aurantii Amari.** *Syn.* ELIXIR OF CURAÇAO.

*Dose* —2 to 4 drachms (8 to 15 ml.)

Oil of bitter-orange 4, tincture of orange 20, alcohol 300, strong orange-flower water 20, syrup 400, distilled water (*s a*) to 1000. Filter through diatomite.

**Spiritus Aurantii Compositus (U.S.P. XI).**

Oils of orange 20%, lemon 5%, coriander 2% and anise 0.5%, in alcohol.

**Oleum Neroli (B.P.C.)** *Syn.* OLEUM AURANTII FLORUM

Obtained by distillation from the flowers of the bitter-orange tree. A pale yellow, slightly fluorescent oil, darkening on exposure to air. Is used largely in perfumery.

**Aqua Aurantii Floris (B.P.C., U.S.P. XI)** *Syn.* AQUA NAPHÆ (*P. Ned. V., P. Helv. V.*)

The triple water diluted immediately before use with twice its volume of distilled water.

**Aqua Aurantii Floris Concentrata (B.P.C.).**

About 1 in 170 of oil of neroli in diluted alcohol. Is approximately 40 times the strength of orange-flower water.

**Aqua Aurantii Floris Triplex (B.P.C.)**

The undiluted orange-flower water of commerce.

**Syrupus Aurantii Floris (B.P.C.)**

*Dose* — $\frac{1}{4}$  to 1 drachm (2 to 4 ml.).

Contains 15% *v/v* of the triple water with sucrose and syrup.

**Syrupus Aurantii Florum (U.S.P. XI).**

Orange-flower water 22.5, sucrose 85, water to 100.

**Succus Aurantii (B.P.C.)** is the expressed juice of the sweet-orange, *Citrus sinensis*. It may be concentrated *in vacuo* to one-seventh of its bulk without loss of vitamin C, and is usually supplied commercially as the concentrate.

**Limonis Cortex (B.P.).** The outer part of the fresh pericarp of *Citrus Limonia*.

The dried peel (*Limonis Cortex Siccatus*) is also used occasionally.

**Syrupus Limonis (B.P.).**

A mixture of syrup with a solution of citric acid in a strong tincture of lemon peel prepared by maceration in alcohol 60%.

**Syrupus Acidii Citrici (U.S.P. XI)**

Tincture of lemon 1, citric acid 1, water 1, syrup to 100

**Tinctura Limonis (B.P.).**

Dose —  $\frac{1}{2}$  to 1 drachm (2 to 4 ml.).

1 in 4, by maceration with alcohol 60%.

**Tinctura Limonis (U.S.P. XI)**

1 part of the outer grated rind of the fresh fruit macerated with  $1\frac{1}{2}$  volumes of alcohol and the residue washed with sufficient alcohol to produce 2 volumes of tincture

**Oleum Limonis (B.P.).**

Dose.—1 to 3 minims (0.06 to 0.2 ml)

The oil expressed from lemon peel. Contains not less than 4% of aldehydes calculated as citral,  $C_{10}H_{16}O$ .

**Oleum Limonis Deterpenatum (B.P.C.).** Terpeneless Oil of Lemon. Is prepared by concentration *in vacuo*, and is both terpene- and sesquiterpene-free. It is about 20 times as strong as oil of lemon

**Succus Limonis (B.P.C.)** is the expressed juice of ripe lemons. It may be preserved with 10% alcohol. It may be concentrated *in vacuo* without loss of vitamin C and is met with in commerce in this form. It contains 7 to 9% of citric acid.

**MYCOTIC INFECTIONS** —Treatment with lemon juice more successful than other treatments. The theory is that the predilection of mycological infections for the palms and soles is due to the alkaline tendency of the sweat in these areas. The patient bathes the affected part night and morning in a pint of hot water to which is added a drachm of strong solution of lead subacetate (this increases the vascular supply), an application of 1% ammoniated mercury in lanolin is then made (to prevent pyococcal superinfection), and the vesicles are then ruptured with a sterilised needle and the parts rubbed four or five times daily with half a lemon from which the peel has been removed. Where irritation is marked, the relief is dramatic. In the later stages, when eczematization has supervened, the lemon juice is diluted or dispensed with and weak tar or ichthammol applications, to which salicylic acid may be added, are employed —K. C. Behsario, *Brit. med. J.*, 1/1936, 406

**Syrupus Succi Limonis (B.P.C.)**

Dose —  $\frac{1}{2}$  to 1 drachm (2 to 4 ml)

A lemon syrup prepared with about 50% *v/v* of lemon juice with a tincture of lemon peel added.

**Acidum Ascorbicum (B.P. Add.).**

**Syn. and Prop. Names.** VITAMIN C, CEVITAMIC ACID, REDOXON (0.05 g tablets) (*Hoffmann-La Roche, London*), CANTAN (0.025 g tablets and 1 ml ampoules) (*Bayer Products, London*), CEBION (*Merck, Darmstadt*, not available in Gt. Britain), PLANAVIT C (*Pharmaceutical Specialities (May & Baker) Ltd., London*).

$O\cdot CO\ C(OH)\cdot C(OH)\cdot CH\ CHOH\cdot CH_2OH = 176.1$ .

Dose — Prophylactic (daily),  $\frac{1}{2}$  to  $\frac{1}{2}$  grain (0.025 to 0.05 g.),

equivalent to 500 to 1000 units, therapeutic (daily),  $1\frac{1}{2}$  to 4 grains (0.1 to 0.25 g.), equivalent to 2000 to 5000 units.

In colourless crystals with an acid taste. Is obtained synthetically or may be extracted from the ripe fruit of *Capsicum annum* or from other vegetable sources. Chemically it is the enolic form of 3-keto-*l*-gulofuranolactone. It contains 20,000 units per g.

**Soluble** readily in water, less soluble in alcohol 95%, methyl alcohol and acetone; insoluble in ether and light petroleum

**Uses.** Is used for the prophylaxis and treatment of scurvy, and has been recommended in a variety of other conditions (*vide infra*).

A reasonable general statement regarding allowable claims for vitamin C would be as follows. An optimum amount of vitamin C should be supplied at all ages for its therapeutic value in preventing the development of acute or latent scurvy. Claims for therapeutic value of vitamin C may be accepted when the agent is described as a corrective measure for scurvy due to a demonstrable absence or a suboptimal quantity in the diet, or in cases in which it is definitely known that there is interference with the absorption of an optimal amount. Advertising of vitamin C for such symptoms as failure to gain in weight or stoppage of growth, anorexia, anæmia, infections, symptoms referable to the central nervous system or hæmorrhagic conditions cannot be accepted unless it is definitely stated that the symptoms are referable to a demonstrable deficiency of vitamin C. The cevitic acid equivalent or potency in terms of International units should be stated in all dosage claims for vitamin C. Cevitic acid (vitamin C) is easily decomposed in presence of certain other substances, therefore, care should be exercised against administering it (or orange juice) in mixtures, or by such procedure as to render it ineffective.—Council on Pharmacy and Chemistry of A.M.A., *J. Amer. med. Ass.*, 1/1936, 1733

**DERMATITIS** Striking effect of *l*-ascorbic acid (vitamin C) on five cases—three of dermatitis produced by arsenobenzene, a case of intolerance to the drug, and a case of gold dermatitis. The good effects of the injections were almost immediately noticeable, and a cure effected in two or three weeks in cases which might have persisted for months or have had even a fatal issue. 0.05 g was given intravenously dissolved in distilled water. In one patient whose dermatitis made it impossible to find a vein, the drug was given orally three times a day with equally good results.—I. Dainow, per *Brit. J. Derm.*, 1936, 48, 167.

**HÆMORRHAGE.**—Five cases of capillary hæmorrhage (essential thrombopenia, purpura infectiosa, essential hæmaturia) satisfactorily treated by intravenous injections of from 100 to 200 mg. daily. Should not attempt treatment in venous or arterial hæmorrhage.—H. Engelkes, *Lancet*, 11/1935, 1285

A case of hæmorrhage in the right eye recurring at intervals of about 20 days and treated by oral administration of vitamin C as a proprietary preparation, Redoxon, cleared up quickly and there was no further remission during several months.—H. Villard and co-workers, per *Nutr. Abstr. Rev.*, Jan., 1936, 744

**PAROXYSMAL HÆMOGLOBINURIA** successfully treated with ascorbic acid, 300 mg. intravenously for several days. The hæmoglobinuria disappeared, and although treatment has now been stopped for 6 weeks paroxysms (due to cold) cannot now be stimulated. Suggested trial in blackwater fever.—L. Armentano, *Nature, Lond.*, 1/1936, 910.

Vitamins in ophthalmology.—John Foster, *Proc. R. Soc. Med.*, 1936, 29, 755  
For further particulars of the chemistry and therapeutics of Vitamin C, see Vol. II.

## AURUM

Au = 197.2.

**Auri Bromidum (B.P.C.).** *Syn.* GOLD BROMIDE.

**Dose.**— $\frac{1}{8}$  to  $\frac{1}{2}$  grain (0.001 to 0.012 g.), or up to  $\frac{1}{2}$  grain (0.03 g.).

Consists of potassium bromaurate,  $\text{KAuBr}_4 \cdot 2\text{H}_2\text{O} = 592.0$ , and occurs as a blackish or brown powder or in brownish-red crystals.

**Soluble** 1 in 5 of water and in alcohol.

**Uses.** In epilepsy, hysteria and migraine, also in nervous dyspepsia, amenorrhœa and chronic Bright's disease. Epileptics treated with it may remain for years free from attacks. Useful in alcoholic neurasthenia, the "Gold Cure" combined with hyoscyamine (or atropine) and strychnine treatment has proved of value.

**Acidum Bromauricum.**  $\text{HAuBr}_4 \cdot 5\text{H}_2\text{O}$  or  $\text{HAuBr}_4 \cdot 6\text{H}_2\text{O}$  In large red needles, m p  $27^\circ$

[P1 81] **Liquor Auri et Arseni Brominatus (B.P.C.)**

**Syn.** LIQUOR AURI ET ARSENI BROMIDI, LIQUOR AURI BROMIDI ARSENIATUS

**Dose.**—5 to 10 minims (0.3 to 0.6 ml.)

Contains in 10 m the equivalent of about  $\frac{1}{4}$  gr of arsenic trioxide and  $\frac{3}{8}$  gr of auric bromide.

**Liquor Auri et Hydrargyri Bromidi.**

**Dose**—5 to 10 minims (0.3 to 0.6 ml.).

Auric bromide, mercuric bromide, of each  $1\frac{1}{2}$  gr, distilled water to 1 oz. Has been used in neurasthenia, epilepsy, syphilis, and acne.

**Auri Trichloridum (Purum)**  $\text{AuCl}_3 = 303.6$  Contains about 65% Au. A brown variety is also made. It contains  $x\text{H}_2\text{O}$ .

**Auri Trichloridum Acidum.** **Syn.** AUROCHLORIC ACID

$\text{AuCl}_3 \cdot \text{HCl} \cdot x\text{H}_2\text{O}$

**Dose**— $\frac{1}{8}$  to  $\frac{1}{4}$  grain (0.001 to 0.004 g), increased to  $\frac{1}{2}$  grain. In brown crystals, contains about 50% of gold. Is deliquescent and easily soluble in water. Has been given as an alternative in phthisis.

**Auri Chloridum (Fr. Cx.).**

**Dose.**— $\frac{1}{8}$  to  $\frac{1}{4}$  grain (0.001 to 0.012 g), or up to  $\frac{1}{2}$  grain (0.03 g.), in a pill massed with kaolin ointment. Hypodermically,  $\frac{1}{16}$  grain (0.003 g.) has been given.

This usually consists of sodium chloraurate (**syn.** Auri et Sodii Chloridum),  $\text{NaAuCl}_4 \cdot 2\text{H}_2\text{O} = 398.1$ , known commercially as "chloride of gold," and contains about 50% of Au. It is an orange-yellow crystalline powder, soluble 1 in 2 of water, only partially soluble in alcohol.

It is sometimes used as a caustic, and is given internally for cirrhosis of the kidney and syphilis. Pills containing  $\frac{1}{16}$  gr. have been found to retard the development of locomotor ataxia, given preferably in monthly courses alternating with arsenic. Combined with strychnine it is useful in neurosis.

Eye affections associated with leprosy, such as conjunctivitis and iridocyclitis, have been treated with this chloride of gold in  $\frac{1}{16}$  gr. doses given intravenously at 10-day intervals for 2 to 4 injections.

LUPUS ERYTHEMATOSUS treated by gold salts intravenously. Of the chloride, 1 ml of 0.1% once a month, increased to 5 ml and if necessary to 10 ml. Results fully equal to those from complex compounds. The latter had annoying sequels not seen with gold chloride. The 0.1% is strongly bactericidal and does not need boiling.—*Brit. med. J. Epst.*, 11/1930, 46.

[P1-81] **Auri et Potassii Cyanidum.**  $\text{KAu}(\text{CN})_2 \cdot 2\text{H}_2\text{O} = 324.3$

Dose.— $\frac{1}{4}$  to  $\frac{1}{2}$  grain (0.001 to 0.02 g.)—*with caution*

White crystalline soluble powder

Has been used in lupus and in syphilis. *Intravenously* the dose was found to be 0.02 to 0.05 g. for adults, and 0.0005 to 0.03 g. for children. To the dose in 1% solution, 50 ml. of normal saline solution are added, and given every second or third day to the extent of 12 injections. The injection is said to be quite painless. After 48 hours a local reaction occurs.

**Auri et Sodii Thiosulphas** (*B.P.C.*). *Syn. and Prop. Names.* AUROBIN (*Richter, London*), SANOCRYLIN (*Dansk Chemo-Therapeutisk Selskab, Copenhagen*; *Napp, London*), CRISALBINE (*Pharmaceutical Specialties (May & Baker) Ltd, London*), SODIUM AUROTHIOSULPHATE  $\text{Na}_3\text{Au}(\text{S}_2\text{O}_3)_2 \cdot 2\text{H}_2\text{O} = 526.5$ .

Dose.— $\frac{1}{2}$  to 15 grains (0.025 to 1 g.) *Intravenously* initially 0.01 g., gradually increasing, if tolerated and no violent reaction, to 0.015 g. per kilo weight *per die*, a maximum of 1 g. per average adult's weight of 10 stone. Solutions must not exceed 5% strength. May also be given *intramuscularly* if intravenous method is inconvenient, *e.g.*, in children. In this case a 3% aqueous solution is used, or a 5 to 10% suspension in oil.

A double thiosulphate of gold and sodium occurring in colourless, odourless stable crystals with a sweet taste. Contains about 37% of Au.

**Soluble** very readily in water, insoluble in alcohol.

**Toxic Reactions.** These are typical of metallic poisoning, and consist of fever, diarrhoea and vomiting with albuminuria and skin reactions of various kinds. In severe cases there may be aplastic anæmia and, rarely, agranulocytosis. Treatment is by sodium thiosulphate, orally or by injection. Mild skin reactions such as localised rashes or papular eruptions usually yield to a few doses of sodium thiosulphate 10 g. given thrice daily.

Dangers greatly exaggerated. With care, rarely causes harm. Has an apparent specific effect on the tuberculous process. Best results in early and pneumonic type.—A. Morland and E. Zimmerli, *Lancet*, 1/1927, 652.

No patient who has had the treatment should be exposed to bright sunlight, as it may result in lilac-coloured pigmentation of the parts exposed.—G. F. Beaumont, *Brit. med. J.*, 11/1928, 819.

**Uses.** Introduced for the treatment of tuberculosis by H. Moellgaard, of Copenhagen, and, although found to have no bactericidal action on tubercle bacilli *in vitro*, is of value particularly in early exudative cases, and as an adjunct to collapse therapy in bilateral cases. Of no use in cases of intestinal tuberculosis or tubercular meningitis. Is also successful in lupus erythematosus, but must be used with great caution and in small dosage in the disseminate type of the affection. Has been used with considerable success in rheumatoid arthritis, preferably administered intramuscularly in oily suspension in doses of 0.1 g. increased by 0.05 to 0.1 g. at intervals of two or three days.

**TUBERCULOSIS.** The treatment shortens the duration of lesser degrees of tuberculosis, and where sufficient tissue with vital energy remains gives good results in more chronic cases. It is extremely dangerous in the more severe forms—it provides a last chance, which, failing, might accelerate death. Early cases of glandular and pulmonary tuberculosis in children well treated, but later stages less amenable.

Local application in surgical tuberculosis beneficial—Leader, *Brit med J*, 1/1925, 176

The M R C. made two Reports on its use Early cases of open infection of the lungs showed some improvement More advanced cases did not stand the treatment well—some were made worse

One death recorded in 140 cases (2 deaths in 30 in the first Report). Risk remains Need for extreme care Patients must be in bed under close control There is definite hope of a drug along these lines—*Brit med J*, 1/1925, 735; *ibid*, 11/1926, 158, *Lancet*, 11/1926, 181

Sanocrysin Research Committee of Japan conclude it is not specific and does not directly destroy the bacillus, but may on occasion be a stimulant in the stationary proliferative type of pulmonary tuberculosis May cause serious damage to tissues Laryngeal and intestinal tuberculosis unsuited for treatment.—*Brit med J*, 11/1928, 349

About 50% of tuberculous patients having a stationary or downward progressive advanced tuberculosis of the "B" or "C" types, when given Sanocrysin in well-regulated doses, will show (1) a rather prompt cessation of symptoms, the changes tending to be permanent if the patient observes the usual measures of hygiene, (2) a clearing of tuberculous infiltration, with marked fibrosis and contraction of cavities, and (3) changes from unfavourable to favourable laboratory findings Of the remainder, about a third show a temporary improvement for a few weeks or months, while the others show no favourable change or prove incapable of tolerating the drug at all Gold therapy may often shorten the convalescent period, prolong life, or both As to selection of cases, it does not seem a matter of duration or stage of disease, so long as the disease is not overwhelming and there are relatively recent discrete tubercles, all of which mean "reactability" on the part of the patient The intravenous injection of gold salts should not be done shortly after a meal, and it is not enough to receive the assurance of the patient that the bowels are regular—K J Hennrichsen and H C. Sweany, *Amer Rev Tuberc (Suppl)*, Oct, 1933, 28

In a total of 1418 cases of pulmonary tuberculosis treated between 1928 and 1933, 60.6%, were ameliorated Gold, in any form yet known, cannot be accepted as a specific treatment—it is inconstant and irregular in its results and there is disparity of effect between one patient and another and even in the same patient at different times At the same time it is a valuable treatment when carefully employed by experienced physicians For the avoidance of untoward reactions it is important that the gold salts should be dissolved in a solution of calcium gluconate It is unnecessary and unwise to stop the treatment after a total of 5 or 6 g has been given the amount may be increased up to a total of 20 or 30 g, advancing with small doses spaced at intervals of one week—L Bernard and C Mayer, *Bull Soc méd Hép Paris*, 1934, 50, 1168

#### LUPUS ERYTHEMATOSUS.

Almost specific Initial dose 0.05 g in 2 ml water, and second injection 5 to 7 days later Injections continued at weekly intervals. Larger doses not advised—*Per J Amer med Ass*, 1/1927, 1111

In 30 cases there were 27 clinical cures and improvement in the remainder. Dose—0.025 g in 2 ml. water once weekly intravenously, increased by 0.005 g. weekly, provided there are no toxic symptoms, up to a maximum of 0.1 g—A J Markley and O S Philpott, *J Amer med Ass*, 11/1929, 235

Of 31 cases treated, 20 (64.5%) were cured Dosage began with 0.05 to 0.1 g., a dose of 0.25 g being seldom exceeded Courses of 8 weekly injections followed by a month or two's rest. Toxic reactions in 18 cases—J L Franklin, *Brit. J Dermat*, 1934, 66

ASTHMA—*Intravenous* injections, starting with a small dose of 0.05 g. and gradually increasing by 0.05 g. Usually not more than 5 injections are necessary. Improvement begins after the second injection and the bronchitis disappears at the end in most cases Kidneys and liver must be sound Fever sometimes occurs but is of short duration Complications avoided by putting patients on a salt-free diet for 3 days, including day of injection—G. P. G. Sobby, *Lancet*, 11/1934, 332

### OTHER PROPRIETARY GOLD COMPOUNDS

**Allochryslne** (*Lumière, Lyons, Anglo-French Drug. Co., London*). Sodium aurothiopropionalsulphonate,  $\text{CH}_3\text{SAuCHOHCH}_2\text{SO}_3\text{Na}$ , containing 35% of gold, issued in concentrated solution containing in 2 ml. 0.2, 0.1 or 0.05 g., together with ampoules containing 8 ml of saline diluent.

For use in all developing cases of rheumatoid arthritis or infective peri-arthritis. Also used in tuberculosis and other indications for chrysotherapy (*vide* Auri et Sodii Thiosulphas).

**Dose.**—A series of 3 intramuscular injections of 0.05 g at 5-day intervals, followed (if no reaction) by weekly injections of 0.1 g to a total of 1.5 or 2 g, then a rest of 6 or 8 weeks followed by a second series with the same rest interval at the end. Then continue by subsequent series of 10 to 20 weekly injections of 0.1 or 0.05 g for a year or two.

**RHEUMATOID ARTHRITIS**—Good results obtained with gold salts, the salts employed being aurothiopropionol sulphionate of sodium, thiosulphate of gold and sodium, thiomalate of gold and sodium, aurothiogluconate and aurothioglycolate of calcium. With small doses at regular intervals and proper selection of cases severe reactions rare. In 500 cases followed up during periods of 2 to 5 years, early cases of under 2 years' duration were cured in the proportion of 50%, the remainder being greatly improved, cases of older standing improved in 80% and cured in 20 to 30%—Jacques Forestier (Aix-les-Bains), *Brit med J*, 1/1934, 350.

100 cases of chronic arthritis treated over a period of 5 years with various gold preparations—Allochrysine, Crisalbine, Myocrisine—12 cases cured, 38 very much improved, 38 improved, and 12 not improved. Few cases escape toxic signs or symptoms, though in the great majority they are slight—H S Pemberton, *Lancet*, 1/1935, 1037.

Severe reactions may be avoided by mixing the Allochrysine injection of 0.1 g. (given intramuscularly) with 10 ml. of 10% calcium gluconate—H J Williams, *Brit med J*, 11/1935, 1098. See also H Roche, *ibid*, 1/1936, 31.

#### **Krysolgan (Schering, London)**

The sodium salt of 4-amino-2-auromer-capto-benzol carboxylic acid,  $C_6H_4NH_2SAuCOONa$ . Contains 50% of gold.

**Dose.**—Initially 0.0001 g intravenously, increased only if and when it ceases to produce a reaction. In general, a dose of 0.05 g should not be exceeded. A pause of at first 10 and later 14 days should be made between injections.

Prevents the growth of the tubercle bacillus in 1 part in a million. Animal results not promising, but clinical results hopeful and inspiring—W E Dixon, *Brit. med. J*, 1/1925, 815. Severe reactions from—*Brit med J Epit.*, 1/1922, 77.

**LUPUS ERYTHEMATOSUS** treated by Krysolgan—H C G Semon, *Brit med J*, 11/1927, 258.

Almost specific and, with ordinary care, not dangerous. Reports of nine cases—six cured—J. H. T. Davies, *Brit. med J*, 1/1929, 12.

Death has followed an injection of 0.001 g. in a case of lupus erythematosus.

**Lopion (Bayer Products, London)** ("G 2949") The sodium salt of the gold derivative of  $\alpha$ -allyl- $\beta$ -4-carboxy-phenyl-thiourea. A water-soluble compound containing about 40% of gold.

**Dose.**—Initially intravenously 0.01 g, routine, 0.1 increasing to 0.5 g.

The gold is concentrated in the liver instead of in the kidneys.

Said to be 10 times less toxic than Krysolgan. Indications as for Sanocrysin. In fresh or extensive disease smaller doses must be employed—*Per Prescriber*, 1929, 250.

#### **Myocrisin (Pharmaceutical Specialities (May & Baker) Ltd, London)**

Sodium aurothiomalate in aqueous solution or oil suspension for intramuscular injection in tuberculosis, rheumatoid arthritis and lupus erythematosus, etc. Available in dry ampoules in various doses from 0.01 to 0.5 g. In rheumatoid arthritis an initial dose of 0.01 g may be followed at weekly intervals by gradually increasing doses until a maximum dose of 0.2 g. is reached, which is continued until a total of 1.5 to 2 g. has been given.

#### **Solganal (Schering, London).**

The di-sodium salt of 4-sulphomethylamino-2-auromer-capto-benzol-1-sulphonic acid,  $C_6H_4O_2N_2Na_2Au$ . An organic compound of gold for intravenous injection for the treatment of tuberculosis, streptococcal infections, multiple sclerosis, infective arthritis, lupus erythematosus and psoriasis. Has also been used in leprosy. Available in dry ampoules, in conjunction with ampoules of solvent, in various doses from 0.01 to 1 g.

**Solganal B and Solganal B Oleosum** are, respectively, a solution and an oily suspension of aurothiogluconate,  $C_6H_4O_2SAu$ , an organic compound of gold, for intramuscular injection. Used for the same purposes as the preceding.

**Solganal Dragées** are prepared containing 0.01 g. and 0.1 g. of Solganal for oral administration in the treatment of infective arthritis. Dose—0.01 g. per day, increased by 0.01 g. each day until 0.1 g. is reached, then given on alternate days, each dose being increased by 0.1 g. to a maximum of 0.6 g. Total to be given in a course, 6 to 8 g.

Treatment of arthritis and rheumatism with Solganal B Oleosum intramuscularly. Of no great value in acute and sub-acute rheumatism in children and contraindicated where severe carditis is present, but superior to other methods in rheumatoid arthritis—G. Slot and co-workers, *Lancet*, 1/1934, 73.

It is not claimed that gold is a specific for every case of arthritis but there is no doubt that in certain groups of cases results are being obtained which are not secured by other means. The usual technique is to give a course not exceeding 1.5 g., at weekly intervals, of Oleosanocrysin, or Solganal B, then a month's holiday, then a second course, then 2 months' holiday, and then a third course. Reactions occur, especially a rash, but with small doses of gold serious results do not seem to occur. Collosol sulphur is used as an adjuvant. Description of 5 cases (osteo-arthritis and rheumatoid arthritis), resistant to other treatment, successfully treated—G. Slot, *Proc. R. Soc. Med.*, Jan., 1936, 224.

As a result of the use of gold treatment (Crisalbine, Solganal B Oleosum, and Lopion) in 374 cases of rheumatoid arthritis, cure or marked improvement occurred in 78% and slight improvement in a further 15%. Reduction in dosage followed by reduction in toxic reaction without sacrificing therapeutic effects. Maximum single dose should not exceed 0.1 g. and total for each course not more than 1.0 g., with at least two courses at an interval of not less than three months. Chrysotherapy the most important form of treatment for rheumatoid arthritis—S. J. Hartfall and H. G. Garland, *Lancet*, 1/1936, 1459.

Chrysotherapy should only be undertaken when the case is severe enough to warrant such a very real risk (of accident), which should be explained to the patient before treatment is instituted—G. J. V. Crosby, *Lancet*, 1/1936, 1463.

**Triphal** (Bayer Products, London). Sodium salt of aurothiobenzimidazocarboxylic acid. Given in doses of 0.025 to 0.2 g. in tuberculosis.

### Colloidal Gold.

Colloidal gold solution may be prepared by the following method:—Neutralise a gold and sodium chloride solution with dilute sodium carbonate solution and adjust the strength to 0.05% Au. With 10 parts of this solution mix 10 parts of a solution containing the calculated amount of formaldehyde required to reduce the gold, reckoning  $3\text{H}\cdot\text{COH}$  to 2 molecules of the gold compound. Employ gelatin as protective. Warm to effect reduction. It can be boiled to sterilise. The finished red hydrosol is to contain 0.025% (1 in 4000) of gold and the same amount of protective.

Dose.—1 to 5 millilitres, 0.00025 to 0.00125 g. or  $\frac{1}{800}$  to  $\frac{1}{160}$  gr approx. of gold, intramuscularly or intravenously. More may be given.

**Uses.** Has been used in the treatment of neurasthenia, alcoholism and morphine addiction. In epilepsy, alcoholic neurasthenia and migraine it has been given hypodermically four times daily (usually 2 ml. divided over the day, but this may be increased) with bitter tonics and digestives, every two hours, *per os*.

Details of remarkable cases. Natural sleep was restored, appetite returned and nervous symptoms disappeared, no ill effects. Addiction of long standing cured—D. E. Stanford Park, *Lancet*, 1/1922, 691, 11/1926, 121. See also *ibid.*, 1/1930, 53.

Tests against control inert isotonic solutions similarly coloured showed that patients treated with gold picked up more rapidly and were more successful—P. Bonsfield, *Lancet*, 11/1925, 1150.

**Orargol** (Anglo-French Drug Co., London). Ampoules of solution of colloidal gold (0.01%) and colloidal silver (0.09%) for intramuscular or intravenous injection. Used in bronchitis, endocarditis and acute articular rheumatism, and also, if used early, for cutting short an attack of pneumonia, influenza or erysipelas.



**AZORUBRUM**

(and other medicinal dyes)

**Azorubrum** (B.P.C.). *Syn.* BORDEAUX B. $C_{20}H_{12}N_2O_7S_2Na_2 = 502.2$ . Colour Index No. 88

The sodium salt of  $\alpha$ -naphthaleneazo- $\beta$ -naphthol-3, 6-disulphonic acid, occurring as a brown powder soluble in water and in alcohol.

**Liquor Azorubri** (B.P.C.). *Syn.* LIQUOR RUBER. 1% w/v in glycerin and chloroform water.

Used as a colouring agent for medicines, 5 m. per oz usually being sufficient

**Congo Red.** *Syn.* SODIUM DIPHENYLISAZOBISNAPHTHYLAMINE-4-SULPHONATE.

*Dose.*—0.25 ml. of 1% solution per kg body weight, by intravenous injection. Solutions should be prepared by adding the powder to sterile water, heating if necessary; they should be used as soon as possible after preparation since the dye hydrolyses slowly in solution

A reddish-brown powder soluble in water. Administered intravenously in the treatment of hæmoptysis and as a diagnostic agent for amyloid disease. Amyloid tissue is readily stained by the dye and the proportion in the blood plasma rapidly falls.

RIGORS avoided by using Grubler's congo red (*Agents Baird and Tatlock, London*), which is free from impurities, made up in freshly prepared solution—J. E. Wallace, *Brit med J*, ii/1934, 881. Preparation of solution with triple-distilled water and filtration through glass wool an important factor in prevention of rigor—J. Libman, *ibid*, 882

**Congo Red** (biologically tested) (*British Drug Houses, London*) is a specially purified form for intravenous administration.

**AMYLOID DISEASE, DIAGNOSIS OF** A comparatively accurate method for the diagnosis of amyloid disease is by intravenous injection of 0.25 ml. per kg of a freshly prepared sterilised 1% solution of Grubler's congo red, the percentage decrease of the dye content of the plasma or serum over a period of one hour being estimated colorimetrically. In normal persons 10 to 30% disappears and in amyloid disease anything between 30 and 100%. Technique described—J. E. Wallace, *Lancet*, i/1932, 391.

A valuable diagnostic measure in amyloidosis. It is possible to obtain a vital staining of amyloid with congo red without harm to the patient, a retention of congo red of from 40 to 100% one hour after injection speaks in favour of the probability of amyloidosis—D. Vivoli, per *J Amer med. Ass*, ii/1932, 87.

**HÆMOPTYSIS.** 5 to 10 ml of a 1% solution of congo red intravenously is a satisfactory hæmostatic—A. J. Scott Pinchin and H. V. Morlock, *Prescriber*, ii/1933, 389.

Intravenously of value in hæmoptysis, the dose being 10 ml. of a 1% solution, repeated if necessary in 4 to 6 hours. The injection is often followed by a rigor of short duration which never gives cause for alarm. Congo red produces an increase in the monocytes, an increase in blood platelets, an increase in blood fibrin content, and a reduction in clotting time—H. V. Morlock and A. J. Scott Pinchin, *Brit. med J*, ii/1934, 763.

Treatment successful in 49 out of 58 cases of tuberculous hæmoptysis.—H. Diaz, per *J. Amer. med. Ass.*, ii/1935, 1228

**HÆMORRHAGE** Intravenous injection of 5 or 10 ml. of congo red is a valuable adjunct in the treatment of hæmorrhage from the urinary tract, e.g., in renal injury, bilateral renal and ureteral calculi, chronic pyelonephritis, vesical calculus, tumour of the bladder, urethral trauma, etc. No untoward effects have followed its use. It has also been employed with marked success in severe epistaxis and hæmorrhage after tooth extraction—R. C. Graves and C. J. E. Kickham, *New Engl J. Med*, 1936, 214, 782.

**Indicarminum** (B.P.). *Syn.* INDIGO CARMINE, SODIUM INDIGOTINDISULPHONATE.  $C_{16}H_8O_8N_2S_2Na_2 = 466.2$ .

*Dose* —By *intramuscular injection*,  $\frac{3}{4}$  to  $1\frac{1}{2}$  grains (0.05 to 0.1 g.); by *intravenous injection*  $\frac{1}{4}$  to  $\frac{1}{2}$  grain (0.008 to 0.016 g.).

The disodium salt of indigotin-5.5'-disulphonic acid, occurring as an odourless blue powder with a coppery lustre.

**Soluble** about 1 in 100 of water; almost insoluble in alcohol 90%. Used as a test for renal efficiency.—*See* Vol II.

**Magenta** (B.P.C.). *Syn.* FUCHSINE, BASIC FUCHSINE, ROSANILINE HYDROCHLORIDE. ANILINE, RED, RUBINE Colour Index No 677.

*Dose* — $\frac{1}{2}$  to 4 grains (0.03 to 0.25 g.), in a pill

Iridescent crystals consisting of a mixture of pararosaniline (Colour Index No. 676) (hydrochloride of triaminotriphenylcarbinol anhydride) and rosaniline (hydrochloride of triaminodiphenyltolylcarbinol anhydride).

**Soluble** in water, and 1 in 8 of alcohol 90%

The aqueous solution is used as a colouring agent and, as carbol-fuchsin, as a stain for *B tuberculosis* (*vide* Clinical and Bacteriological Notes, Vol. II)

Given in renal albuminuria.

**Unguentum Fuchsin** 5% in soft paraffin Has been used in carbuncle and soft chancre. Also useful for impetigo

**Fuchsin Paint** (*Castellani*)

Epidermophytosis of the toes (Mango toe) and other forms of epidermophytosis well treated with a paint consisting of saturated alcoholic solution of basic fuchsin 10 ml, 5% phenol solution 100 ml. Filter and add boric acid 1 g, after 2 hours add acetone 5 ml, 2 hours later add resorcinol 10 g. Keep in dark-coloured stoppered bottles. Should be employed initially with care and in small amount.—Sir A. Castellani, *Lancet*, ii/1928, 596

**Carbol-fuchsin** paint, with 2.5% of salicylic acid added, the best treatment for epidermophytosis. Rub the *nails* thoroughly with the paint twice daily, even after the disease seems to have subsided. Three months' treatment is required for a cure.—J. Hasson, *Brit med J*, ii/1934, 928

**Acid Fuchsin** (Colour Index No 692) is a mixture of the sodium or ammonium salts of di- and tri-sulphonic acids of magenta. **Soluble** in water and alcohol 90%.

**Rosaniline** (*Syn.* ROSFINE) **Acetate**.  $C_{20}H_{11}N_3$ ,  $C_2H_3O_2 \cdot 5H_2O = 451.3$

Dark red crystals **soluble** in water and in alcohol. Both this compound and magenta are sometimes called "roseine"

**Methylviola** (B.P.C., *P. Helv. V*). *Syn.* METHYL VIOLET, METHYL ROSANILINE, PYOKTANIN. Colour Index No 680.

In green crystalline powder consisting of a mixture of the hydrochlorides of principally tetra-, penta-, and hexamethylpararosanilines. There are numerous methyl violets, the particular shade depending on the degree of methylation.

**Soluble** 1 in 20 of water, 1 in 20 of alcohol 90%, 1 in 16 of glycerin, and in oleic acid. Insoluble in liquid paraffin

Dilute solutions have been injected locally and applied for malignant growths, but crystal violet, a purified methyl violet, is now generally used

**Viola Crystallina** (B.P.C.). *Syn.* CRYSTAL VIOLET, METHYL-ROSANILINE, MEDICINAL GENTIAN VIOLET (*vide infra*), HEXAMETHYLPARAROSANILINE HYDROCHLORIDE. Colour Index No 681.

**Dose**—0.003 to 0.007 gramme per kilo body weight (= 3 to 7 grains for a 10-stone man) intravenously in a  $\frac{1}{4}$  to 1% aqueous solution.

**GENTIAN VIOLET.** According to the Colour Index, commercial gentian violet, as supplied in Gt. Britain, is a mixture of methyl violet and dextrin. For medicinal purposes it should be free from dextrin and in *N.N.R.* is described as a mixture of penta- and hexamethylpararosanilines. Since the tetra-, penta- and hexa-compounds show no appreciable difference in therapeutic effect, while the hexa-compound, crystal violet, is most readily obtained pure, the latter is usually intended when gentian violet is required in medicine.

Greenish-bronze crystals or powder

**Soluble** 1 in 20 of water, 1 in 16 of glycerin, 1 in 20 of alcohol 90%. The dye is precipitated from aqueous solution by sodium chloride and other electrolytes.

**Uses.** A powerful antiseptic with selective action on gram-positive organisms. It is employed intravenously in septicæmia and endocarditis. Has been tried in encephalitis.

For *direct application* a solution 1-500 to 1-1000 has been recommended, for instillation 1-10,000, and for *intravenous injection* 5 mg. per kilo-weight, injected in 0.5% solution.

Encouraging results have been obtained in acute infections of joints by lavage and direct medication. Also in post-influenzal empyema by intrapleural instillation of 1-10,000 to 1-1000 solutions.

**BURNS**—A 1% solution gives excellent results. Without preliminary cleaning of burned area the dye is sprayed on at 2-hour intervals for the first few hours. No dressing applied but surface exposed to air and protected by a cradle. An eschar is rapidly formed and spraying is then performed every 4 to 6 hours during the day till healing is complete. Analgesia almost instantaneous—*Lancet*, 1/1933, 484.

A jelly prepared by the addition of 30 g. of tragacanth to 1000 ml. of 1% solution gives superior results to an aqueous solution in the treatment of burns—J. H. Connell, *J. Amer. med. Ass.*, 1/1933, 1220.

**ENCEPHALITIS.**—Recovery in three cases, also in one of chorea—*Proc. J. Amer. med. Ass.*, 11/1925, 1670.

**ENDOCARDITIS**—Review of literature (entirely American) on the subject of intravenous injections of the dye. Details of 7 cases of rheumatic carditis so treated, all children, varying from 5 to 13 years. **Dose**—25 to 50 ml. of a 0.25% aqueous solution (i.e., 0.005 g. per kilo). Injections given at weekly intervals. Definitely toxic effects occurred in the case of a 5-year old child. Of 10 cases, 8 were definitely improved. With caution as to dose and type of case, the method is safe and worth further trial in the treatment of blood infections—William Gunn, *Lancet*, 1/1927, 127.

Subacute infective endocarditis. Good result with 1 in 500 aqueous solution.—R. H. Major, *Brit. med. J. Epit.*, 1/1925, 38.

Malignant endocarditis treated disappointing. 1% aqueous solution used. Except for intense cyanosis of short duration, no untoward symptoms produced.—*J. Amer. med. Ass.*, 11/1926, 1677.

**PERNICIOUS ANÆMIA.**—Gentian violet *per os*, 5 to 50 ml. of a 1 in 1000 solution after meals, or in 1 to 2½ grain capsules or tablets, gave a rise in hæmoglobin content and in erythrocyte count, and in some cases amelioration of symptoms. Vomiting, nausea, or diarrhoea may be caused—*Med. J. Rec.*, 1927, 9.

**SKIN AFFECTIONS.**—Infectious eczematoid dermatitis, impetigo, folliculitis and furunculosis. A 5% solution in water containing 20% alcohol, applied with a swab.—A. R. McFarland, *Arch. Derm. Syph.*, N. Y., Jan., 1928.

**STAPHYLOCOCCAL SEPTICÆMIA.**—Startling results may be obtained, but failures are equally numerous. The cases reported total about 40% definitely improved, 20% possibly improved and 40% unimproved. Used in 1 in 200 solution in water, each ml containing 0.005 g of dye, a full dose being 45 ml. for a 7-stone patient. More concentrated solutions may cause thrombosis. Initial injection of 0.002 g per kilo. Sharp temperature reaction, sometimes a chill, following injection. In favourable cases, following fall in temperature, improvement is marked. Value due to its bacteriostatic action in the blood stream—W D Gatch, H M Trusler and J E. Owen, *J Amer med Ass*, ii/1925, 894.

In sepsis, when Gram + staphylococci are the sole or predominant ætiological organisms and when bacteria are accessible to blood stream, gentian violet intravenously is most beneficial. May be given in safety in doses varying from 0.003 to 0.007 g per kilo in a 0.25 to 1% solution—Per *J Amer med Ass*, ii/1925, 300.

Doses of less than 0.003 g per kilo of little, if any, value. Several injections at intervals of one or several days often necessary—Per *J Amer med Ass*, ii/1926, 442.

**THRUSH** treated with local use of 1% aqueous solution. Apparent cure in one day or less in 50% of cases. Relapses on stopping treatment occasionally to be expected—*J Amer. med Ass*, ii/1925, 901.

**Liquor Tinctorium (B P C)** *Syn* BONNEY AND BROWNING'S SOLUTION, BLUE PAINT, SOLUTION OF BRILLIANT GREEN AND CRYSTAL VIOLET.

Crystal violet and brilliant green 0.5% w/v of each in equal parts of alcohol and water.

A non-irritant antiseptic for sterilising the skin. Stains may be removed with hypochlorite solution, *e g* eusol.

**Methylthioninæ Hydrochloridum (B P, U S P XI)** *Syn* METHYLTHIONINE CHLORIDE, METHYLENE BLUE, METHYLENUM CÆRULEUM (*P. Helv V, Fr Cx, P Jap IV*), TETRAMETHYLTHIONINI CHLORIDUM (*P. Belg. IV*).  $C_{16}H_{18}N_3ClS = 319.7$

*U S P XI, P. Helv V, and Fr Cx* have  $3H_2O$ .

*Dose.*—1 to 5 grains (0.06 to 0.3 g.) in pill, cachet or capsule; or hypodermically, 1 grain. *U S P XI average dose*  $3\frac{1}{2}$  grains.

Dull dark green crystals, forming an intense blue solution in water.

**Soluble** about 1 in 50 of water, soluble also in alcohol 90% and chloroform.

**Incompatible** with caustic alkalis.

*Distinguish from the commercial compound with zinc*

**Uses.** Mildly antiseptic and excreted by kidneys, hence used as genito-urinary antiseptic in cystitis, gonorrhœa and vesical catarrh. Is also used in these conditions by injection, as 0.1 to 0.2% solution. It has also been given internally in malaria where quinine is not tolerated and in blackwater fever. It is a feeble analgesic and was formerly advocated for rheumatism, migraine and painful nervous affections. Colonic lavage with the 1 in 5000 to 1 in 1000 solution has been used in dysentery and ulcerative colitis.

In chronic suppurative otitis media and conjunctivitis, 1 in 500 solution is instilled warm. In intertriginous eczemas, 3 to 5% solution. It has been used in bilharziasis. The 5% solution, injected intramuscularly in 1 ml. doses, is used as a test for renal efficiency (*see Vol. II*). *It colours urine blue, and fæces become blue on exposure to air.*

Cyanide poisoning has been successfully treated by injecting intravenously 100 ml. of a 1% solution.

**CYANIDE POISONING**—Methylene blue should be tried in every case of cyanide poisoning and should be part of emergency equipment. Amyl nitrite and sodium tetrathionate may also be used, the former even in conjunction with methylene blue. The balance of evidence is against methylene blue being of any value in CO poisoning.—G. F. Copper, *U S Nav med Bull*, Wash., 1935, 33, 364.

**MALARIA**—Specially useful in cases refractory to quinine. *Dose*—0.05 g. in 5 ml. water, from two to five doses during the day intravenously—well tolerated, or by the mouth up to a total of 1.5 g. taken during meals. Subcutaneously may cause abscess.—Per *J Amer med Ass*, 11/1926, 712.

**Tabellæ Methylthioninæ Hydrochloridi (B.P.C.)** Contain 2 gr. (0.12 g.)

**Methylene Blue Compound, Horwitz (Lilly, London)** Methylene blue 1 grain, copalba 1½ m., East Indian santal oil 1½ m., methyl salicylate ½ m. *Dose*.—1 or 2 capsules thrice daily after meals. In the early stages of gonorrhœa.

**Novaurantia (B.P.C.). Syn. ORANGE G.**

$C_{16}H_{10}N_2O_7S_2Na_2 = 452.2$  Colour Index No. 27

The disodium salt of benzeneazo-β-naphthol-6 : 8-disulphonic acid, occurring as a yellowish-red powder, *soluble* in water and in alcohol 90%, giving orange coloured solutions.

**Viride Malachitum (B.P.C.). Syn. MALACHITE GREEN**

Colour Index No. 675  $2C_{23}H_{25}N_2 \cdot 3H_2C_2O_4$

The oxalate of *pp'*-tetramethyldiaminotriphenylcarbinol anhydride, in green crystals with metallic sheen. Soluble in water and alcohol 90%. Has antiseptic properties, especially for gram-positive organisms, but brilliant green is now usually preferred.

Stains on the hands with malachite green are easily removed by rubbing with a little cotton wool soaked in alcohol, dilute hydrochloric acid or dilute acetic acid.

**Uses.** During the war was much employed as an antiseptic wound dressing—especially as spray. Is more active for gram-positive organisms.

**Cheate's "Green Spray."** *Syn. SUBLIMATE MALACHITE GREEN SOLUTION.*

Equal parts of 2% malachite green in 80% alcohol and 2% mercuric chloride in 80% alcohol. The two solutions are best kept separate and mixed as required.

The spraying must be thorough and the spirit allowed to evaporate before applying the dressing. *Must not be applied to mucous membranes.*

[P2 81] **Pigmentum Viride (St. J. H.)**

Malachite green 5 gr., mercuric chloride 5 gr., industrial methylated spirit 6 dr., water to 1 oz.

**Viride Nitens (B.P.C.). Syn. BRILLIANT GREEN**

Colour Index No. 662.  $C_{27}H_{33}N_2 \cdot SO_4H$ .

The sulphate of tetraethyldiaminotriphenylcarbinol anhydride, in small golden crystals soluble in water and alcohol 90%.

**Uses.** The dye has been much used for the same purposes as acriflavine.

These two dyes had the highest "T.C." (*v. Acriflavine*). Brilliant green differs, however, in that it is not advised to be introduced by injection into closed spaces, and its activity is reduced in the presence of serum. It is also less rapid in action. It differs from crystal violet in being strongly bactericidal to the coli-typhoid group. For wounds a 1 in 1000 to 1 in 2000 solution is used,

promoting a vigorous growth of granulation tissue. It may also be used for continuous irrigation of wounds. Septic conditions of the ears have been treated with brilliant green  $\frac{1}{2}\%$ , mercuric chloride  $\frac{1}{2}\%$  in 90% alcohol, and the 0.1% aqueous solution with 0.25% of allantoin is used as ear drops to promote epithelisation after the radical mastoid operation.

It is a useful epithelial stimulant in various minor injuries and affections, *e g*, impetigo, indolent ulcers of various kinds, blisters, etc.

Stains on the skin can be removed with spirit, those on clothes by spirit or washing with soap.

**EPIDERMOPHYTOSIS**—Painting of the affected part daily with 1% brilliant green in rectified spirit of value.—W Lambert, *Brit med J*, 1/1934, 798

**SYCOSIS**—Remove crusts with 5% salicylic ointment, followed by epilation of loose pustule-encircled hairs and daily painting with 1% alcoholic solution of brilliant green in 70% alcohol. 53 cases cured after 12 to 25 applications, with no relapses.—*Lancet*, 1/1932, 202

**Brilliant Green Ointment.** Brilliant green 1 or 2% in twice the amount of alcohol 90% and incorporated with soft paraffin. For superficial wounds

**Brilliant Green Paste (Hey's).** Brilliant green 1, boric acid 275, French chalk 25, liquid paraffin 200. The dye is incorporated in solution in a little spirit. For filling wound cavities

**Methyl Green**, *syn* LIGHT GREEN, is chloromethylhexamethyl-*p*-rosaniline hydrochloride.

**Rubrum Scarlatinum (B P C).** *Syn* BIEBRICH SCARLET R MEDICINAL, SUDAN IV, *o*-TOLUENEAZO-*o*-1-TOLUENFAZO- $\beta$ -NAPHTHOL. Colour Index No. 258.  $C_7H_7N_2 \cdot C_7H_6N_2 \cdot C_{10}H_6OH$ . A red dye with m.p. between 165° and 185°

**Soluble** in oils and fats, insoluble in water

**Uses.** To regenerate skin and to hasten epithelisation, has been much employed as ointment

There has been some confusion regarding the nomenclature and constitution of the scarlet R dyes, and the above *medicinal* Biebrich should always be specified

**INDOLENT ULCERS**—The following dressing applied at least twice daily recommended. Immerse lint for two days in a solution of 20 grains of Biebrich red in a pint of water with 2% powdered allantoin. Allow to dry without wringing or artificial heat and then iron out at low temperature. Cut to size and shape of ulcer.—J M Barbour, *Brit med J*, 1/1928, 382.

[P1 81] **Oleum Scarlet et Atropinae.** Corneal ulcers have been treated by a 5% suspension in castor oil containing 1% atropine.

**Unguentum Rubri Scarlatini (B P C)** *Syn* UNGUENTUM RUBRUM.

5% in simple ointment. Other strengths (from 2 to 8%) are sometimes used.

The following scarlet colours have been similarly employed.

**Oil Scarlet.** *Syn* CERASINE RED, BENZENEAZOBEN/ENEAZO- $\beta$ -NAPHTHOL, SUDAN III.

This is also insoluble in water, moderately in alcohol, and very soluble in chloroform and ether and has been found quite satisfactory

**Non-Staining Scarlet.** *Syn* *o*-AMINOAZOTOLUENE

Soluble in oils and fats, insoluble in water. Considered by some to be more efficacious than scarlet red

**"Ordinary" Biebrich scarlet** is the sodium salt of *p*-sulphobenzeneazo-*o*-sulphobenzeneazo- $\beta$ -naphthol, soluble in water making an orange-red solution

**Diacetylaminoazotoluol** (*P. Helv. V, P. G. VI, P. Svec X*).

$CH_3 \cdot C_6H_4 \cdot N \cdot N \cdot C_6H_4 \cdot CH_3$ ,  $N(CO \cdot CH_3)_2$  = 309.2.

Red powder with slight acetous odour. Insoluble in water, soluble in alcohol, ether or chloroform, also in oils, fats, and soft paraffin. A non-staining compound

used for the same purposes as scarlet red. Usually applied as a 2% ointment in soft paraffin.

Azodermin, the monacetyl derivative of aminoazotoluol, has also been used for promoting the growth of skin on wounds

**Pellidol** (*Bayer Products, London*) An ointment containing 2% of diacetyl-aminoazotoluene in soft paraffin basis For promoting epithelial growth.

**Trypan Red.** *Syn* SODIUM 3-SULPHODIPHENYLDISAZOBIS- $\beta$ -NAPHTHYLAMINE-3,6-DISULPHONATE. Colour Index No. 438 A brown powder giving a red aqueous solution

Is active against trypanosomes *in vitro*, but rarely used medicinally

**Trypan Blue.** *Syn* SODIUM DITOLYLDISAZOBIS-8-AMINO-1-NAPHTHOL-3,6-DISULPHONATE  $C_{22}H_{14}O_4N_4S_2Na_2$  Colour Index No 477 A bluish-grey powder giving a violet solution

Successful in piroplasmiasis, *biliary fever* or *malignant jaundice* of the dog (canine piroplasmiasis) and *red water* or *Texas fever* of cattle (bovine piroplasmiasis) It is stated to be a certain and immediate cure for distemper *Dose*—Dogs 2 months old, of 3 to 5 lbs weight, 3 ml to 4 ml of  $\frac{1}{2}$ % solution From 10 lbs to 60 lbs weight, dose ranges from 3 to 20 ml of saturated solution (1% approx) Subcutaneously, or in preference intravenously, into the vena saphena in the hind leg of a dog Cattle—*Dose*—100 to 200 ml of saturated solution.

**PARKINSONISM** Successfully treated by trypan blue 1% intravenously—2 injections of 1 ml followed by 3 or 4 of 2 ml with an interval of 3 or 4 days between each two injections and an interval of a month between courses No ill effects and injections well tolerated—*Lancet*, 1/1932, 1319

**Tartrazina (B.P.C.).**  $C_{10}H_6O_6N_4S_2Na_3 = 534.2$ .

Colour Index No. 640.

The sodium salt of 4-*p*-sulphobenzeneazo-1-*p*-sulphophenyl-5-hydroxypyrazole-3-carboxylic acid, occurring as an orange-yellow powder Is used as a colouring for lemonade and lemonade powders, and, in conjunction with orange G, as a yellow colour for foods and medicines.

**Liquor Tartrazinæ Compositus (B.P.C.)** *Syn.* LIQUOR FLAVUS.

Tartrazine 0.75% *w/v* and orange G, 0.25% *w/v*, in glycerin and chloroform water. Used as a yellow colouring agent for mixtures, etc.; 5 m per oz. is approximately equivalent to  $12\frac{1}{2}$  m of fresh tincture of saffron.

**Auramine.** *Syn* TETRAMETHYLDIAMINODIPHENYLKETONIMINE HYDROCHLORIDE  $C_{17}H_{18}N_4Cl \cdot H_2O = 303.7$

*Dose*— $\frac{1}{4}$  grain (0.02 g) has been given *per os*

A yellow powder soluble in water The solution is decomposed on boiling or on long standing in the cold, the imino group of the compound being converted into a ketone group by hydrolysis, giving the insoluble Michler's ketone and ammonium chloride

An antiseptic non-irritant dye for sterilising the skin prior to operation

**SEPTICÆMIA.**—Auramine 0.1 g intravenously on the first two days and 30 ml. of antistreptococcal serum subcutaneously on the first three days—J E R McDonagh, *Brit med. J.*, 1/1928, 693.

**Glauramine** (*British Drug Houses, London*) is a concentrated solution of auramine in glycerin and alcohol, to be diluted with water immediately before use

**Sudan Red III.** AMINOAZOBENZENE- $\beta$ -NAPHTHOL.

$C_{22}H_{18}N_2O = 352.2$  A brown dye for colouring fats, and in histology

**Chrysoidine.** DIAMINOAZOBENZENE HYDROCHLORIDE.

$C_8H_8N_2 \cdot C_6H_4(NH_2)_2 \cdot HCl = 248.6$ . An orange dye, slightly soluble

### Other Common Colouring Matters

**Anchusa (B.P.C.).** *Syn.* ALKANNA, ALKANET ROOT.

The dried root of *Anchusa tinctoria* (Boraginaceæ). Contains 3%

red amorphous substance, alkannin. "Red oil" is obtained by macerating alkanna in liquid paraffin 1 in 7

**Coccus (B.P.)** *Syn* COCHINEAL, COCCUS CACTI

The dried female insect *Dactylopius coccus* (Hemiptera) containing eggs and larvæ. The insects are reared on various species of *Nopalea* (Cactaceæ). If killed by sulphur or charcoal fumes the insects are silvery in colour ("silver grain") owing to deposit of wax on the surface. If killed by heat the wax is melted and "black grain" cochineal is produced.

**Liquor Cocci (B.P.C.)** contains the colouring matter of 10% w/v of cochineal

**Tinctura Cocci (B.P.)** *Dose* —5 to 15 minims (0.3 to 1 ml) 1 in 10 of alcohol 45%

**Carminum (B.P.C., P. Helv. V)**

Red colouring matter containing about 50% of carminic acid,  $C_{14}H_{14}O_{10}$  = 382.1, prepared from cochineal by precipitation with alum. It is insoluble in water, but entirely soluble in aqueous ammonia. Is used to colour medicinal and toilet preparations and for staining in microscopy.

**Liquor Carmini (B.P.C.)** contains 6% w/v of carmine in a weakly ammoniacal solution. For colouring mouthwashes, etc., 3 or 4 minims per fl. oz. is used.

**Glycerinum Carmini (B.P.C.)** is a similar solution prepared with potassium carbonate.

**Liquor Rosæ Dulcis (B.P.C.)** is a similar preparation of 4% w/v of cochineal containing oil of rose. Is useful for colouring and perfuming preparations.

**Crocus (B.P.C., P. Helv. V)** *Syn.* SAFFRON. The dried stigmas and tops of the styles of *Crocus sativus* (Iridaceæ). It is a curious old delusion that saffron tends to bring out the rash of measles. Its preparations are used as colouring agents.

**Glycerinum Croci (B.P.C.)** 1 in 40 in glycerin and alcohol 60%.

**Syrupus Croci (B.P.C.)** Glycerin of saffron 1, syrup 7. About 1 in 8 is sufficient for colouring mixtures.

**Tinctura Croci.** 1 in 5 of alcohol 60%.

## BALSAMUM PERUVIANUM

*B.P., U.S.P. XI, P. Helv. V, P. Dan.*

*Dose* —5 to 15 minims (0.3 to 1 ml)

A balsam exuded from the trunk of *Myroxylon Pereiræ* (U.S.P. XI, *Tolunfera Pereira*), after beating and scorching. Occurs as a viscid liquid containing cinnamoin and cinnamic acid.

**Soluble** in chloroform, partially soluble in ether, light petroleum and glacial acetic acid; soluble 1 in 1 of alcohol 90%, but solution becomes turbid on adding 2 of alcohol 90%. Insoluble in water. Inhalation of the vapour from a few drops of a solution of balsam of Peru 1 in alcohol 2, in a little hot water, is useful in pharyngitis. As a dressing to wounds, if aseptic, may be left for 20 days if necessary. Scabies has been treated with a paint of balsam 3, glycerin 1. But test for albumin in urine both before and during treatment.

[P1] **Lotio Balsami Peruviani**—MacNaughton Jones suggested in alopecia a preparation of Peru balsam 1 dr., spirit of rosemary 1 oz., tincture of cantharides 4 dr., pilocarpine nitrate 2 gr., almond oil 1 oz. This is applied at night and washed off next morning with a borax and spirit lotion.



**Unguentum Peruvianum (B.P.C.).** 12½% in simple ointment.

**Unguentum Balsami Peruviani.** Wyatt Wingrave's formula Balsam of Peru 20, Trikresol 5, soft paraffin *q s* to 100. Mix warm.

For scabies an ointment containing Peruvian balsam and sublimed sulphur 4½% of each, in soft paraffin—W. Knowsley Sibley (Treatment of Skin Diseases)

**Mencièrè's Solution, *q v*,** contains Peruvian balsam

**Ammoniacum (B.P.C.).**

**Dose.**—5 to 15 grains (0.3 to 1 g.).

Gum-resin from *Dorema Ammoniacum* (Umbelliferae) In pale yellow tears or nodular masses with characteristic odour and acrid taste. Is used in chronic bronchitis with viscid secretion to facilitate expectoration.

**Mistura Ammoniaci (B.P.C.)**

**Dose.**—½ to 1 ounce (15 to 30 ml).

Contains the equivalent of 13 gr. of ammoniacum per oz

**Balsamum Tolutanum (B.P., U.S.P. XI, P. Helv V, P. Dan.)**

**Dose.**—5 to 15 grains (0.3 to 1 g.)

Obtained from the trunk of the *Myroxylon Toluifera* (U.S.P. XI, *Toluifera Balsamum*) (Leguminosae). Recently prepared is soft, but becomes brittle in cold weather.

**Soluble** 1 in 1 of alcohol 90%, and in ether, chloroform and solutions of fixed alkalis, usually leaving some residue

Is antiseptic and expectorant

**Liquor Tolutanus (B.P.C.)** 1 part mixed with 7 parts of syrup gives a preparation similar to syrup of tolu (B.P.)

**Syrupus Tolutanus (B.P.)** **Dose**—½ to 1 drachm (2 to 4 ml)

Made by digesting the balsam and water on the water-bath during ½ hour and dissolving sucrose in the filtered liquid

**Syrupus Balsami Tolutani (U.S.P. XI)** *Syn.* SYRUPUS TOLU, U.S.P. X **Average dose**—2½ drachms (10 ml). Tincture of tolu balsam 5, sucrose 82, water to 100

**Tinctura Tolutana (B.P.)**

**Dose.**—½ to 1 drachm (2 to 4 ml). 1 in 10 In mixtures the resin must be suspended with mucilage

**Tinctura Balsami Tolutani (U.S.P. XI)**

**Average dose.**—30 minims (2 ml.)

Balsam of tolu in alcohol, 1 in 5

**Tussispect (Beiersdorf, Welwyn Garden City)** Ammoniated primula saponin 0.03%, aqua tolu 38.765%, tinct. aurant. 1%, ol. anis 0.2%, sugar 60% Cough expectorant

**Balsamum Gurgunae.**—Gurjun Balsam, Wood Oil. **Dose.**—½ to 2 drachms. Obtained from *Dipterocarpus turbinatus* and other species. Contains from 40 to 80% of volatile oil, and is used in gonorrhœa and as an expectorant given with malt extract.

**Styrax (B.P., U.S.P. XI, P. Helv. V).** *Syn.* STYRAX PRÆPARATUS, BALSAMUM STYRAX LIQUIDUS (P. Dan.).

**Dose.**—10 to 30 grains (0.6 to 2 g.). The balsam obtained from the wounded trunk of *Liquidamber orientalis*, purified by dissolving in alcohol, filtering and evaporating. U.S.P. XI allows it to be obtained also from *L. styraciflua*. A thick brown liquid containing not less than 30% of balsamic acids. Contains cinnamyl cinnamate (styracin) and other cinnamic acid compounds together with a large proportion of storesin,  $C_{36}H_{55}(OH)_2 = 538.5$ .

**Soluble** in alcohol 90%, ether, carbon disulphide, chloroform and glacial acetic acid.

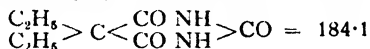
Is used as an ointment containing 20 to 25% in scabies and parasitic skin diseases.

[P2] **Storaxol** (*Parke, Davis, London*) Storax, resorcinol, menthol, camphor, phenol (22 gr per oz), and precipitated sulphur in a wool fat and soft paraffin base For use in acne, sycosis, etc

## BARBITONUM

B P, P G VI, Fr. Cx. Supp 1920, P. Helv. V, P Jap. IV, P Ned. V, P Svec. X, P Dan., U.S.P. XI, P. Belg. IV, F.F. VIII, P Ital. V

Syn and Prop Names 5 : 5'-DIETHYLBARBITURIC ACID, DIETHYL MALONYL UREA, MALONUREA, BARBITALUM, MALONAL, HYPNOGEN (*Fragner, Prague*), VERONAL (*Bayer Products, London*).



[P1] "Barbituric acid, its salts; derivatives of barbituric acid; their salts; compounds of barbituric acid, its salts, its derivatives, their salts, with any other substance"

[81] "Barbituric acid, its salts, derivatives of barbituric acid, their salts; compounds of barbituric acid, its salts, its derivatives, their salts, with any other substance"

[84] "Barbituric acid, its salts, derivatives of barbituric acid, their salts; compounds of barbituric acid, its salts, its derivatives, their salts, with any other substance"

**Dose.**—5 to 10 grains (0.3 to 0.6 g.)—should be taken with a hot drink.

P G VI max single dose 0.75 g, max per diem 1.5 g; Fr. Cx. Supp, P. Belg. IV and F.F. VIII, 0.5 and 1 g. respectively, P. Ital. V, 1 and 2 g. respectively.

**Caution.**—5 grains is sufficient for an ordinary case of insomnia 50 gr. might be regarded as the average minimum fatal dose, although as little as 10 gr. has proved fatal.

**Manufactured** by condensing urea with ethyl diethylmalonate

A white crystalline powder melting at 189° to 192° (U.S.P. XI 187° to 190°).

**Soluble** 1 in about 170 of water, 1 in 12 of boiling water, 1 in 8½ of alcohol 90%, 1 in 25 of ether, 1 in 35 of chloroform. Boiling with alkalis decomposes it Also soluble in acetone and ethyl acetate

**Uses.** Soporific in nervous restlessness, insomnia and depression, for maniacs and in cardiac trouble. Does not affect temperature or respiration. May cause erythema Produces sleep without subsequent depression Tolerance to it may be established in some cases. For insomnia it should be taken 2 hours before retiring.

Barbiturates do not relieve pain, and in insomnia due to this cause they are given in combination with an analgesic such as amidopyrine.

If a phenyl group,  $C_6H_5$ , is used to replace one of the ethyl groups in barbitone, the drug seems to acquire special depressant power over the motor cortex (e.g., Luminal in epilepsy).

If sodium is added to the barbituric nucleus without disturbing the essential ring formation the product becomes soluble, giving greater speed in action and allowing of its injection (e.g., Sodium Soneryl, Sodium Amytal, Sodium Evipan).

The introduction of bromine into the barbituric nucleus (as in Pernocton) acts as a preventive to the state of excitement sometimes preceding narcosis —N. Mutch, *Brit med J*, 1/1934, 321.

The margin of safety between the hypnotic dose and the lethal dose as represented by the ratio M.L.D./M Th D. is Luminal 1/3, Barbitone 1/6, Soneryl, Nembutal and Phanodorm 2/4, Dial 2/5, Evipan 5. It would not appear very safe to employ Luminal in full hypnotic doses —N. Mutch, *Brit med J*, 1/1934, 321.

**Contraindications**, or indications for special caution, are old age, genitourinary disease, liver disease, advanced disease of heart or lungs, severe toxæmia, and idiosyncrasy.—R. D. Gillespie, *Lancet*, 1/1934, 337.

Owing to the risk of pneumonia in individuals receiving large doses of barbiturates, they should be withheld in the presence of inflammation of the lungs, operations for empyema and in catarrhal conditions of the bronchial and upper air passages. Also when efficiency of the liver or kidneys is affected by toxic blood conditions, by local inflammation of these organs, or by other diseases such as eclampsia or cirrhosis —H. W. Featherstone, *Brit med J*, 1/1934, 326.

**Toxic Effects.** Barbitone is excreted slowly, and bowels and kidneys should be functioning adequately. It is cumulative, and regular administration may cause chronic poisoning characterised by headache, visual disturbance and weakness, with anæmia and albuminuria. Acute poisoning is characterised by a brief period of headache, ataxia and muscular twitching, followed by sleep rapidly passing to coma. Later the breathing becomes slow and shallow, there is œdema at the bases of the lungs, and bronchopneumonia may set in. Nystagmus is frequently present, and there is complete suppression of urine. In a few individuals idiosyncrasy exists, and quite small doses produce skin eruptions of various kinds.

#### DANGERS OF THE BARBITURIC HYPNOTICS

Reasons of Veronal poisoning—its potency, no evidence of habit, delayed action, and that in every case of death the victim has tried to procure immediate sleep—G. Archdall Reid, *Brit med. J.*, 1/1925, 630.

Recovery after taking as a single dose about 200 grains of Veronal. Complete unconsciousness lasted 113 hours and there were other grave symptoms —S. M. Wells, *Brit. med. J.*, 11/1927, 826.

Death from probably 50 grains of Veronal taken for sleeplessness in the belief by the victim that he could take more than most people—A. Deane, *Brit. med. J.*, 11/1927, 192.

A man of 120 pounds (54 kg.) bodyweight survived a total dose of 18 g (270 gr.) of sodium barbital, taken with suicidal intent. The poisoning was characterised by a deep coma of six days' duration, a very high temperature and rapid pulse and respiration, in contrast to the usual picture of severe depression of temperature and respiration.—D. K. Chang and M. L. Tainter, *J. Amer. med. Ass.*, 1/1936, 1386.

Veronal taken every night is liable to produce mental and moral changes with suicidal tendencies, also diplopia with visual paralysis and the kind of speech found in G.P.I.: a characteristic feature of Luminal is hæmatoporphyrinuria. Continued administration of these drugs produces pathological changes in the central nervous system, which, although they usually disappear when dose is discontinued, may become permanent. The resemblance between the

comatose condition produced by them and the condition of normal sleep is only superficial, and under these drugs the margin between sleep and fatal coma in cats is a very narrow one. There is definite evidence of cumulative action, and tolerance is never established.—Sir Wm. H. Willcox, *Brit med J*, 1/1927, 877; *Lancet*, 1/1927, 1037

Repeated daily administration of barbitone and allied drugs over long periods is not always free from danger, and may induce serious toxic symptoms in the central nervous system. Repeated use also induces addiction, and addicts not uncommonly take a dangerous overdose, accidentally or otherwise. Confusion having been caused by an initial dose, the patient may continue to take further and possibly fatal quantities without realising the danger.

The treatment of acute barbitone coma is materially improved by cisternal drainage.—Sir J. Purves-Stewart and Sir W. Willcox, *Lancet*, 1/1934, 500

The alleged dangers of the barbiturates. Statistical tables giving details of all fatalities associated with barbituric drugs recorded up to the end of 1932. Of the total of 5147 recorded suicides in 1931 only 13, or 0.26%, were attributed to barbiturates, but, in view of the amount of publicity these cases have received, a fashion in barbiturate suicides may be expected in the near future. Up to the end of 1932 there is no case on record in which barbiturates, either a single dose or repeated doses of therapeutic magnitude, have caused death in the absence of complicating factors.—R. D. Gillespie, *Lancet*, 1/1934, 337

"The Battle of the Barbiturates." A protracted and voluminous correspondence.—See *Lancet*, 1/1934

Toxicology of barbiturates.—H. T. Roper-Hall, *Proc. R. Soc. Med.*, Jan., 1936.

**Antidotes to Barbiturate Poisoning.** Empty stomach by stomach tube, using 2 gallons of warm water, as emetics probably of little use. Keep patient warm and try to keep him awake, but he must not be walked about. Give hot, strong coffee. Strychnine,  $\frac{1}{4}$  gr., Coramine, 5 to 15 ml of 25% solution, and alcohol, should be injected and repeated as required. Fluids must be given freely; if coma is prolonged, patient must be fed by stomach tube with coffee, dextrose, peptonised milk, etc. Dextrose in saline may be given by rectum, and saline intravenously. Artificial respiration should be started early and kept up for a long time. Oxygen with 7% carbon dioxide inhalations may be necessary. Lumbar and cisternal puncture and drainage to remove the poison may be carried out every 12 or 24 hours, especially if "veronal pneumonia" has set in.

Veronal is excreted slowly and unchanged in the urine. In cases of poisoning increase the efficiency of the kidneys by injection of large volumes of 5% to 10% dextrose solution. A woman who had taken 60 grains was given  $1\frac{1}{2}$  litres 5% dextrose 4 hours later. In 6 hours she passed 1100 ml urine, and 11 hours later showed no symptoms of the drug.—*Amer J Pharm*, 1930, 599

A fatal case in which 62 cg of strychnine were given without any signs of intoxication by it.—L. Raymond and J. Delay, per *Lancet*, 1/1934, 93

Alcohol injections intravenously of value. A patient in a state of slight coma from having taken 1.5 g of Gardenal was given 20 ml of 30% alcohol intravenously once an hour, and awoke to complete consciousness on the fourth injection. Animal results confirmatory of clinical observations. Probably at least 30 ml of 30% alcohol should be given hourly till patient wakes.—Prof. Carnière, C. Huriez and P. Willoquet, *Bull Acad. Méd.*, No. 18, 1934, per *Lancet*, 1/1934 1243

The prevalence of barbiturate poisoning has shown a sudden increase in France since 1930—a single hospital had 62 cases in 18 months, and it is estimated that there must be thousands of cases of greater or less severity every year. The increase in severe cases is due to the fact that the barbiturates (particularly Luminal) are becoming the method of choice for suicide among certain classes. Treatment by large doses of strychnine,  $\frac{1}{4}$  to  $\frac{1}{2}$  gr., repeated hourly if necessary, with Coramine injections or carbogen (oxygen and carbon dioxide) inhalations as respiratory stimulants.—C. Flandin, F. Joly and J. Bernard, per *Brit med J*, 11/1934, 263.

Treatment of acute barbiturate poisoning by washing out stomach with animal charcoal and sugar-lime; Coramine injected, camphor for convulsions; large doses of strychnine intravenously; oxygen inhalations, infusions with adrenaline and insulin.—Hans Fischer, *Schweiz. med. Wschr.*, 1935, 65, 441

Use of Coramine in barbiturate poisoning —*Pr. méd.*, 1935, 43, 465; Killian, *Brit. med. J. Epit.*, 1935, 97.

[P1 81 84] **Tabellæ Barbitoni** (B.P.C.). Contain 5 grains (0.3 g.).

[P1 81 84] **Tabellæ Barbitoni et Amidopyrinæ** (B.P.C.).

*Dose.*—1 tablet. Contains 2 gr. of barbitone and 4 gr. of amidopyrine.

[P1 81 84] **Beitol** (Continental Laboratories, London) Tablets containing barbitone, valerian, and hyoscyamus. Also in solution and in ampoules. In nervous and mental conditions.

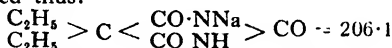
[P1 81 84] **Chineonal** (Merck, Darmstadt, Martinsdale, London) is quinine diethylbarbiturate. *Dose*—10 grains (0.6 g.) for adults. In fevers, neuralgia, etc.

[P1 81 84] **Codeonal** (Knoll, Ludwigshafen, Pharmaceutical Products, London) A combination of codeine diethylbarbiturate (2 parts) with sodium diethylbarbiturate (15 parts) in powder or 2½ gr. tablets. Hypnotic, in diseases of the nervous system and pulmonary disorders. It takes effect after about half an hour.

[P1 81 84] **Veramon** (Schering, London) A combination in tablet form of amidopyrine and a molecular compound of one molecule of amidopyrine with one molecule of barbitone. Analgesic in neuralgias, migraine, dysmenorrhœa, biliary colic, and all forms of pain. *Dose*—Adults, 1-2 tablets, children, ½-1 tablet. The effect sets in after about 20 minutes and lasts for 4-5 hours.

[P1 81 84] **Veropyron** (Richter, London) Tablets containing barbitone 0.15 g., amidopyrine 0.35 g. *Dose*—1 or 2 tablets.

[P1 81 84] **Barbitonum Solubile** (B.P.) *Syn. and Prop. Names* BARBITALUM SOLUBILE (U.S.P. XI, P. Helv. V, P. Ned. V), MEDINAL (Schering, London) (P.G. VI, P. Svec. X, P. Ital. V), VERONAL-SODIUM (Bayer Products, London). Graphically it may be represented thus.—



*Dose*—5 to 10 grains (0.3 to 0.6 g.) dissolved in water either before or not less than 1 hour after meals. In most cases 5 grains is sufficient for an adult. P.G. VI has max. single dose 12 grains approx. (i.e., the same as for barbitone).

Hypnotic effect is also obtained by the use of suppositories medicated with 0.4 to 0.5 g.

Even small doses, e.g., 1 grain 3 times a day, in some instances, produce a lengthy sleep—at night.

It is stated that toxic signs do not appear with less than 15 grains daily, whilst an adequate sedative effect at the menopause is obtained with 1 to 2 grains 3 times a day, half an hour after meals.—J. H. Hannan, *Practitioner*, 11/1927, 263.

**Manufacture.** Rub down barbitone 184 g. in a mortar with about 200 ml. of water, and then add sodium hydroxide pure, 40 g. previously dissolved in water *q.s.* and *estimated*. It should be as free from CO<sub>2</sub> as possible. Evaporate to dryness on water bath. It may be regarded as an acid salt. If a proportion of alkali sufficient to make the di-sodium body is used, decomposition sets in on drying.

White crystals **soluble** 1 in 6 of cold water; slightly soluble in alcohol 90%, insoluble in ether or chloroform. It has properties and uses similar to barbitone *antea*. It is useful in sea-sickness.

**Incompatible** with ammonium salts, *e.g.*, the bromide, and with acids, also with chloral hydrate. In preference, give it alone.

Solutions of soluble barbitone decompose on heating, forming crystals of diethylacetyl urea,  $(C_2H_5)_2CO \cdot NH \cdot CO \cdot NH_2$ . If the compound is prepared with more than the minimum quantity of alkali, solutions decompose below  $100^\circ$ , otherwise they will withstand short heating at  $100^\circ$  and can be sterilised by tyndallisation but not by autoclaving.—A. E. Bailey, *Pharm J.*, 1/1936, 620.

**Pharmacology.** Magnesium chloride 2 parts combined with sodium barbital 1 part hastens onset and lessens persistence of narcosis without appreciably increasing toxicity.—H. G. Barbour and W. F. Taylor, *J. Pharmacol.*, July, 1931, 331.

Animal experiments show that fear and excitement definitely diminish the soporific action of soluble barbitone.—*Pharm J.*, 1/1925, 444.

[P1 81-84] **Tabellæ Barbitoni Solubilis (B.P.C.)** contain 5 gr. (0.3 g.).

[P1 81 84] **Neurinase (Genevrier, Neuilly; Wilcox, Jozeau, London).** Preparation of soluble barbitone and extract of valerian. 1 dr contains 3 gr of soluble barbitone and  $\frac{1}{2}$  gr of extract of valerian. **Dose.**—1 drachm in the morning and 1 to 4 drachms at bedtime. For nervous insomnia and neurasthenia.

[P1 81 84] **Veronigen (Hewlett, London)** **Dose**—1 drachm (4 ml) diluted, about 1 hour before going to bed. For nervous sleeplessness in children 10 to 20 minims diluted. A liquid preparation of barbitone as hypnotic.

[P1 81 84] **Dipropylbarbituric Acid.** *Syn* PROPONAL.



**Dose**—2 to 8 grains (0.12 to 0.5 g.). More poisonous than barbitone. Very narrow margin between therapeutic and toxic dose.

[P1 81 84] **Butylethylbarbituric Acid.** *Syn and Prop. Name.* NEONAL (*Abbott, Chicago*; not available in Gt. Britain), BUTO-BARBITAL.



**Dose.**—1 to 2 grains (0.06 to 0.12 g.) produces sleep in half an hour; in addition, it has marked analgesic properties. It may be given at any time, but in no case less than  $\frac{1}{2}$  hour after food. A larger dose, *e.g.*, 3 grains (0.2 g.) gives a deep sleep lasting some time. In pain from wounds 3 to 4 grains may be used. In delirium 2 grains. Max. in 24 hours, 4 grains.

A white, crystalline powder with slight bitter taste. Soluble 1 in 300 of water. Sedative and hypnotic for use in insomnia and as basal narcotic. Said to be three times as active as barbitone.

[P1 81-84] **Soneryl Tablets (Pharmaceutical Specialties (May & Baker) Ltd., London)** contain  $1\frac{1}{2}$  gr. of butylethylbarbituric acid.

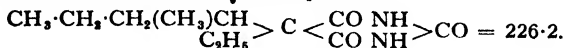
[P1 81 84] **Soneryl Sodium** is the sodium derivative of Soneryl, and is available in capsules containing 0.15 g. ( $2\frac{1}{2}$  gr. approx.). For basal narcosis and in obstetrics.

A reliable basal hypnotic producing sleep or drowsiness in 95% of cases when administered by mouth one hour before the induction of general anaesthesia. Optimum dose varies from 0.6 to 0.9 g. *per os*. Depression of respiration in a few instances and restlessness in 10% of cases. Has not been given in senility, pulmonary disease, renal impairment or arteriosclerosis.—S. E. Birdsall, *Brit med. J.*, 1/1933, 871.

[P1 81-84] **Sonalgin (Pharmaceutical Specialties (May & Baker) Ltd., London)** Tablets containing Soneryl  $1\frac{1}{2}$  gr. and phenacetin  $3\frac{1}{2}$  gr.

[P1-61-64] **Nembutal** (*Abbott, Montreal; Pharmaceutical Products, London*). *Syn.* PENTOBARBITAL SODIUM, SODIUM *iso*-AMYTAL, SODIUM ETHYLMETHYLBUTYLBARBITURATE.

The acidic substance has the composition:



The sodium salt may be indicated thus



A white, crystalline powder, with slightly bitter taste. Very soluble in water, freely in alcohol, practically insoluble in ether. Aqueous solutions are alkaline to litmus.

*Dose.*—As a hypnotic  $1\frac{1}{2}$  gr. *per os* or *per rectum* is sufficient. As a pre-anæsthetic and basal hypnotic give one capsule ( $1\frac{1}{2}$  gr.) the evening before and one or two 30 minutes before operation. In obstetrics, the usual dose is 4 or 5 capsules (6 to  $7\frac{1}{2}$  gr.) in primipara, and 3 in multipara, given after there is definite dilatation of the cervix with definite and regular uterine contractions at not more than 5-minute intervals. For intravenous or intramuscular use to control convulsions in strychnine poisoning and tetanus, or in emergency operations, not more than  $7\frac{1}{2}$  grains are dissolved at the time of use in 10 ml. of water, and injected at the rate of 1 ml. per minute.

Intravenous injections must be made fresh. Undesirable to boil—*Brit med. J.*, 1/1931, 359.

When given as a pre-anæsthetic in young children, suppositories have been found better than oral or intravenous administration, the dosage, excluding children of 1 year, being 1 grain per year up to a total of 6 grains for children of 6–8. After 8 the drug may be given orally. The suppositories take from 2 to 4 hours to act. Used successfully in 200 cases with no unpleasant after-effects.—R. Jarman, *Brit. med. J.*, 1/1936, 236.

ANTIDOTES TO SUBLETHAL AND LETHAL DOSES OF PENTOBARBITAL, CHLORAL HYDRATE AND AVERTIN. The order of practical usefulness of the several therapeutic measures, judged by the degree of improvement in respiration, circulation and reflex excitability, degree of shortening of the usual stages of recovery and the margin of safety of effective dosages of each agent, from high to low, is as follows. picrotoxin, Metrazol, ephedrine, artificial respiration, Coramine, Icoral, strychnine and caffeine sodio-benzoate. The most satisfactory therapeutic measures included combined medication with ephedrine and either picrotoxin, Metrazol or Coramine. Tolerance to these preparations parallels the degree of depression present, particularly with the convulsants. The dosage and frequency of administration of the antagonists must be gauged by the duration of the optimal response observed and the relative need for supportive treatment. Artificial respiration, especially with gas mixtures containing 5 to 10% of carbon dioxide, is highly effective as a single resuscitation measure against lethal doses of these hypnotics.—O. W. Barlow, *J. Pharmacol.*, 1935, 66, 1.

Nembutal is a renal poison. The kidneys stop excreting, with consequent suppression of urine. Four cases of fatal suppression of urine from doses of Nembutal of less than 10 grains. The only thing that will save a person with pneumonia due to barbituric acid drugs is lumbar puncture and the draining off of a good deal of cerebrospinal fluid—Sir W. Willcox, *Brit med J.*, 1/1933, 144.

It would appear to be extremely unwise to administer morphine or Omnipon in conjunction with basal narcotics. Two deaths—one with Avertin plus  $\frac{1}{2}$  gr. of morphine and  $\frac{1}{160}$  gr. of hyoscine, hypodermically, and one with Nembutal

(orally) with morphine  $\frac{1}{2}$  gr. and atropine  $\frac{1}{10}$  gr.—J. M. McNeill Love, *Brit. med. J.*, 1/1934, 327.

Danger almost non-existent if not more than  $\frac{1}{2}$  gr. of morphine is given.—G. Keynes and C. L. Hewer, *ibid.*, 400.

**Uses.** A "basal hypnotic," the supplementary anæsthetic being nitrous oxide and oxygen, with addition of ether when necessary. The sedative effect continues for 1 to 5 hours after operation. Intravenous injection bridges the gap between consciousness and unconsciousness before general anæsthesia, it also lessens the amount of anæsthetic required, diminishes or obviates post-operative nausea. The chief disadvantage is post-operative restlessness in about 10% of cases.—I. W. Magill, *Lancet*, 1/1931, 74.

Order of hypnotic efficiency (in conjunction with nitrous oxide)—Nembutal, Avertin, Phanodorm, Pernocton. Avertin safest, but efficiency decreased owing to short duration of narcosis.—O. W. Barlow and co-workers, *J. Pharmacol.*, Apr., 1931, 377.

Placed in the following order of merit as basal hypnotics—Nembutal, Sodium Amytal and Pernocton. Nembutal the most outstanding anæsthetic drug to date.—I. W. Magill, *Lancet*, 1/1931, 353.

As basal pre-anæsthetic hypnotic Nembutal intravenously in 108 cases—better than Amytal or Pernocton. Effect can be increased by giving morphine simultaneously.—S. Rowbotham, *Lancet*, 1/1931, 439.

Basal anæsthetics and allied substances—their use and misuse.—H. W. Featherstone, *Brit. med. J.*, 1/1934, 322.

Oral Nembutal is a great boon as a basal anæsthetic in children. The dose should be small (1 grain or less for a child of 4), given when possible at night, so that the child falls asleep in bed and general anæsthesia can be induced without waking him. The powder may be dissolved in a teaspoonful of syrup or cane sugar in warm water, to mask the bitter taste. If the barbiturate is not effective, or is vomited, a very small dose of Avertin (e.g., 0.05 g. per kilo) may be given. Of value for such procedures as the setting of fractures, repeated lavage of nasal sinuses, and multiple operations for cellulitis or pyæmia.—H. W. Featherstone, *Brit. med. J.*, 1/1934, 324.

**CHILD BIRTH.** Combined oral use of Nembutal and chloral hydrate gave 62% of painless labours in 60 cases without ill-effects to mother or children. Initial dose (when os uteri is two-fifths dilated and regular pains present) Nembutal 3 gr., chloral hydrate 30 gr. (in 3 oz. of sweetened home-made lemonade). First "repeat" dose of  $1\frac{1}{2}$  gr. and 30 gr. respectively after 2 hours, and subsequent similar doses at 3-hourly intervals, to a total of  $7\frac{1}{2}$  and 120 gr., in 12 hours. Chloral given 10 minutes after Nembutal to obviate vomiting. Not contraindicated in heart disease or albuminuria. May be given by midwives.—J. V. O'Sullivan and W. W. Craner, *Lancet*, 1/1932, 119.

Nembutal and chloral the most reliable means for obtaining complete amnesia in labour for the practitioner who cannot spend many hours with his patient.—A. M. Claye and D. W. Currie, *Lancet*, 1/1932, 1175.

From an analysis of 100 cases it is concluded that Nembutal, given in combination with chloral, is of undoubted value, especially in placid women with strong distressing pains. Best given between 3 and 5 hours before delivery. Of very doubtful value in nervous or hysterical patients. Nembutal 3 gr. in capsules by the mouth, followed by chloral hydrate 22 gr. as a syrup, perfectly safe. Repeat dose, Nembutal  $1\frac{1}{2}$  gr. and chloral hydrate 22 gr., in 3 hours.—F. C. Kelly, *Lancet*, 11/1933, 693.

**MENTAL CONDITIONS.**—NEMBUTAL SUPPOSITORIES. Of value in all types commonly seen in a mental hospital. Individual response tested by preliminary dose of 2 gr. at bedtime—usually resulting in 6 hours sleep. In certain manic states the dose needs to be increased to 6 grains, which is safe and usually effective. Most valuable in the treatment of acute anxiety states and good results in agitated melancholia and senile confusion.—J. S. Horsley, *Brit. med. J.*, 1936, 283.

**TETANUS.** Several cases of tetanus have been controlled by intravenous Nembutal at least two with a successful cure.—H. W. Featherstone, *Brit. med. J.*, 1/1934, 325.

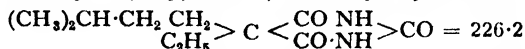
[P1 §1 §4] **Pentothal Sodium** (Abbott, Montreal; Pharmaceutical Products, London). Originally known as thio-barbiturate 8064.

An intravenous anæsthetic supplied in ampoules of 1 g. with ampoules of 10 ml. distilled water.



It is a yellow crystalline powder and, when dissolved in water, produces a gaseous solution which takes a moment or two to clear. It is important to see there is no precipitate. It is used as an intravenous anæsthetic, 3 ml. usually being sufficient for minor operations. It may be given either as a single dose (for an operation likely to last 10 to 20 minutes), in repeated doses (a second or even third dose may be given), or by continuous intravenous infusion. The induction period is as dramatic, smooth and pleasant as with Evipan, without the twitching or jactitation seen with the latter, and with less fall in blood pressure. The main disadvantage is that it is more depressant to the respiratory centre. Gross hepatic disease or jaundice is a contraindication. The recumbent position is the safest for administration. Pre-medication with barbiturates not advisable. Coramine the most reliable antidote in case of collapse. Used in over 1000 cases—R. Jarman and A. L. Abel, *Lancet*, 1/1936, 422.

[P1-81 84] **Amytal** (*Lilly, London*) is isoamylethylbarbituric acid,



Supplied in tablets containing  $1\frac{1}{2}$  or  $\frac{3}{4}$  gr, also in crystal form.

A white, crystalline powder, with slightly bitter taste; soluble in alcohol and ether; very slightly in water; insoluble in paraffin hydrocarbons. M.p.  $153^\circ$  to  $155^\circ$ . Saturated aqueous solutions are acid to litmus.

**Dose**—As sedative,  $\frac{1}{4}$  to  $\frac{3}{4}$  grain (0.02 to 0.04 g.) at 2-hour to 4-hour intervals, with water or hot milk. As hypnotic,  $1\frac{1}{2}$  to 5 grains (0.1 to 0.3 g.), 1 to  $1\frac{1}{2}$  hours before retiring. As local or general anæsthetic, 3 to 10 grains (0.2 to 0.6 g.) according to age, etc. As antispasmodic in tetanus to control convulsions, 6 to 12 grains (0.4 to 0.8 g.)

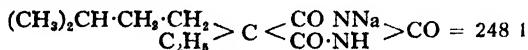
**Uses.** A sedative and hypnotic in the control of insomnia and as a preliminary to surgical anæsthesia. It is stated not to be excreted in the urine and not to affect the kidneys.

A hypnotic rather than a true anæsthetic. May be combined with spinal anæsthesia—J. T. Mason and J. E. Baker, *Lancet*, 1/1930, 1302.

**In obstetrics**, 30 mg. per kilo body weight per rectum produces effective anæsthesia and amnesia, with little, if any, effect on the baby—D. L. Drabkin, *J. Amer. med. Ass.*, 11/1929, 1175; see also *ibid.*, 1339.

[P1 81 84] **Amytal Compound** (*Lilly, London*) Capsules containing amytal  $1\frac{1}{2}$  gr and amidopyrine  $3\frac{1}{2}$  gr. Sedative and analgesic.

[P1-81 84] **Sodium Amytal** (*Lilly, London*) is sodium isoamylethylbarbituric acid.



Supplied in capsules containing 1 gr. or 3 gr., and in ampoules containing 0.125, 0.25, 0.5 or 1 g.

This ureide is isomeric with Nembutal. It is a white, friable, hygroscopic, odourless, granular powder with slightly bitter taste; very soluble in water, about 1 in 1 of alcohol 90%, and practically insoluble in ether.

**Dose.**—As sedative or hypnotic in capsules containing 3 grains (0.2 g.), *per os*, repeated if necessary at 6-hour intervals. As antispasmodic in tetanus, 6 to 12 grains (0.4 to 0.8 g.) to control convulsions.

It is also given by the following methods:

**Rectally** not exceeding 15 grains (1 g.), with a maximum of 1.5 g. in 3% aqueous solution, followed immediately by injection of 1 or 2 ounces of water.

**Intravenously** has been given in dose of 5 to 15 grains (0.3 to 1 g.) in 10% solution at rate of 1 ml. per minute. Blood pressure has to be watched continuously. There are many contraindications, and should only be given by this route when oral administration is not feasible.

**Intramuscularly** not more than 5 ml. of 10% solution should be injected at any one point.

As a pre-anæsthetic the dose is from 3 to 10 grains (0.2 to 0.6 g.)—but only safe for use for this purpose (and in tetanus) by experienced workers familiar with the literature.—*N.N.R.*, 1936.

**Uses.** Primarily, as hypnotic for basal narcosis. Also as general hypnotic and in obstetrics

Average fatal dose orally for dogs 125 mg. per kilo; rectally and intravenously in 10% solution, 200 and 70-75 mg. per kilo respectively.—E. E. Swanson and H. A. Shonle, *J. Pharmacol.*, Feb., 1931, 305.

Causes marked drop in blood pressure intravenously. Unconsciousness lasts 3 to 6 hours. Safer *per os* or *per rectum*. In medicine, useful for the control of convulsions in unmanageable cases and as a specific for strychnine poisoning (extensive American bibliography).—L. G. Zervas, *Brit. med. J.*, 11/1930, 897, *Lancet*, 11/1930, 693.

Risk of insufficient pulmonary ventilation in period of sleep (24-48 hours) after operation, and a large number require catheterisation.—J. T. Mason and J. E. Baker, *per Lancet*, 1/1930, 1302.

**GASTRIC AND DUODENAL ULCER** treated. Checks secretion of gastric juice.—L. G. Zervas, *Brit. med. J.*, 11/1930, 527.

**LABOUR.** Best procedure in women of average weight  $\frac{1}{2}$  to  $\frac{1}{4}$  gr. of morphine,  $\frac{1}{16}$  to  $\frac{1}{8}$  gr. of scopolamine, and 6 to 9 gr. of Sodium Amytal intramuscularly, when contractions are regular and occurring at less than 10-minute intervals—injections repeated as indicated. Intravenous injections given at beginning of second stage of 6 to 10 gr. during several pains, and stopped when patient is well controlled. Rapid in action and has a wide range of safe dosage. No harm to mother and labour not delayed.—A. R. Robbins, *J. Amer. med. Ass.*, 11/1929, 1251.

Amytal and Sodium Amytal as analgesics in confinements. 3 grains at first, late in first stage of labour. If necessary repeat in 4 hours.—*Lancet*, 11/1930, 1086.

Sodium Amytal in labour not well spoken of. Morphine and nitrous oxide or rectal Avertin in preference.—J. Riddell, *Lancet*, 1/1931, 162.

[P1 81 84] **Phanodorm** (Bayer Products, London). CYCLOHEXYNETHYLBARBITURIC ACID; known in U.S.A. as PHANODORN (Winthrop Chemical Co., New York).



**Dose.**—Average dose 1 tablet (3 grains). In mild insomnia,  $1\frac{1}{2}$  grains; obstinate insomnia, 3 to 6 grains. Larger dose not repeated in less than 12 hours.

A white, crystalline powder, with bitter taste; soluble in alcohol and ether, only slightly soluble in water.

**Uses.** As hypnotic. In nerve affections to be taken in warm water. Is stated to be more rapidly eliminated than barbitone.

[P1 81-84] **Hebaral Sodium** (Parke, Davis, London). Known as Ortal-Sodium in U.S.A. The sodium salt of normal hexylethyl barbituric acid. **Average dose.**—1 to 2 capsules of 3 grains each. Hypnotic and sedative.

[P1-81-84] **Evipan** (*Bayer Products, London*). *N*-methyl-*C*-*C*-cyclohexenyl-methylmalonylurea.

*Dose*.—For insomnia, 1 to 1½ tablets in half a glass of water.

[P1-81-84] **Evipan Sodium** (*Bayer Products, London*). The sodium salt of Evipan. For intravenous "short" anæsthesia and induction anæsthesia.

**Toxic Effects.** Fatalities recorded elsewhere are probably due to overdosage. A series of over 5000 cases without mishap is recorded. No stage of analgesia is to be relied on after injection of Evipan—*Arch klin Chir*, 1933, 716.

Details of 6 fatalities—G. Slot and A. H. Galley, *Brit med J*, ii/1934, 204.

A case of late paralysis due to Evipan administration—J. V. Landor and M. Salleh, *Brit med. J*, ii/1934, 940. See also F. B. Mallinson, *ibid*, 1025.

Most authorities lay stress on the advisability of slow injection—J. Blomfield, *Med. Annu*, 1935, 21.

**Contraindications.** Should be avoided in severe liver embarrassment or in depression of the respiratory centre. In cases where it is contraindicated but is still thought the safest method of anæsthesia, it should be given alone without other drugs, with cautious dosage and preliminary injection of atropine to counteract tendency to œdema of lung. Facilities for administering oxygen and CO<sub>2</sub> mixtures should be at hand—G. Slot and A. H. Galley, *Brit med J*, ii/1934, 204.

Provided it is not administered single-handed, nor to patients in the upright position, nor to old or feeble subjects, and provided an adequate airway is maintained, it has a very large scope in the field of safe and useful anæsthesia—R. Jarman and A. L. Abel, *Lancet*, i/1934, 512.

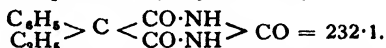
**REFERENCES.** Not to be regarded as a basal hypnotic in the sense that Nembutal and Avertin are, owing to its evanescent action. As a preliminary, it should be classed rather with nitrous oxide and ethyl chloride. It is an admirable method of inducing anæsthesia for those who like intravenous methods. Excitement, restlessness and after-effects are rare, and it is a reliable anæsthetic for minor surgery, and is thus a valuable agent in the case of persons gravely ill for whom a short anæsthesia is desired. It is less efficient than Nembutal by the mouth, but is a useful hypnotic to break the habit of sleeplessness—Anæsthetics Committee, M.R.C., *Brit. med J*, ii/1933, 63.

A method of minimising respiratory depression when using soluble barbiturates (e.g., Evipan or Nembutal) intravenously, by the incorporation of a respiratory stimulant in the same solution with the anæsthetic. Starting with a solution of the barbiturate, made so that each 1 ml. of the solution contains 100 mg. of barbiturate, 25 mg. of the stimulant (Coramine) is added to each 1 ml. of the solution. The needle is kept in the vein throughout the operation, and the same principle of intermittent administration is utilised as is employed in the semi-open method of administration of ethyl ether. To ensure that respiratory exchange is taking place a fluffy piece of cotton is fastened to the upper lip by a narrow piece of adhesive tape. Patency of the airway must be maintained by sustaining the lower jaw. Encouraging results obtained.—J. S. Lundy, *Proc Mayo Clin*, 1935, 791.

To use Evipan in a casual manner is to court disaster, and a thorough examination should be made in order to exclude hepatic disease, low blood-pressure, or other pathological conditions. The recovery period is so uncertain that it is essential to watch the jaw until consciousness returns. On its introduction Evipan was hailed as a panacea for all dental anæsthetic difficulties, but time has tempered this enthusiasm; we now know that it does not monopolise the anæsthetic field, but is a splendid addition if we realise its limitations, and that what is gained by steadiness of anæsthesia may be lost by restricted flexibility. It is a light anæsthetic, having the advantage of ease of induction over gas and oxygen, but it is doubtful if it is really better than the older methods, and in the case of really extensive operations there are no advantages. It is now recognised that its use should be restricted to those with a sound knowledge of drugs and general anæsthetic routine, and its simplicity should not tempt the operator to give his own injections. All the advantages may be offset by chest complications caused by respiration depression, and occasionally there is excitement necessitating supervision for many hours, while the stupor which sometimes follows makes it difficult to judge as to the rallying of the patient, thus making excessive

demands upon the nurses, as the patient must be watched continuously to avoid obstruction of the breathing.—H. T. Roper-Hall, *Proc. R. Soc. Med.*, Jan., 1936, 276.

[P1 81 84] **Phenobarbitonum (B.P.).** *Syn. and Prop. Names.* 5-PHENYL-5-ETHYLBARBITURIC ACID, PHENYLETHYLMALONYL UREA, PHENOBARBITALUM (*U.S.P. XI, P. Helv. V*), ACIDUM PHENYL-ÆTHYLICOBARBITURICUM (*P. Ned. V, P.G. VI, P. Svec. X, F.E. VIII, P. Dan.*), LUMINAL (*Bayer Products, London*), GARDENAL (*Pharmaceutical Specialities (May & Baker) Ltd., London*).



*Dose.*— $\frac{1}{2}$  to 2 grains (0·03 to 0·12 g.). More is sometimes given; where there is much excitement, 5 to 6 grains up to 12 grains (0·8 g.), the maximum dose as given in *P. Belg.*; *U.S.P. XI* average dose  $\frac{1}{2}$  grain. A white powder, melting at 173° to 177°.

*Soluble* about 1 in 1000 of water, 1 in 15 of alcohol 90%, 1 in 40 of ether, 1 in 50 of chloroform. Readily soluble in aqueous alkali hydroxides and carbonates.

*Uses.* Hypnotic in conditions of excitement, in sleeplessness associated with pain, migraine, chorea, children's convulsions and in mental conditions, etc. Bowels to be kept open and kidneys in good working order.

*For references to its use, and toxic effects, see under Phenobarbitonum Solubile.*

[P1 81 84] **Elixir Phenobarbitoni (B.P.C.)**

*Dose*—1 to 2 drachms (4 to 8 ml.).

A flavoured preparation containing  $\frac{1}{2}$  gr. of phenobarbitone per drachm.

[P1 81 84] **Tabellæ Phenobarbitoni (B.P.C.)** contain  $\frac{1}{2}$  gr. (0·03 g.).

[P1 81 84] **Tabellæ Phenobarbitoni et Theobrominæ (B.P.C.).** *Prop. Names.* THEOGARDENAL TABLETS (*Pharmaceutical Specialities (May & Baker) Ltd., London*), THEOTONE TABLETS (*Allen & Hanburs, London*), THEOMINAL TABLETS (*Bayer Products, London*).

*Dose.*—1 or 2 tablets.

Phenobarbitone  $\frac{1}{2}$  gr. and theobromine 5 gr. For high blood pressure, angina pectoris and menopausal disorders.

[P1 81 84] **Alepsal (Genevrier, Neuilly; Wilcox, Jozeau, London).** Tablets containing phenobarbitone  $1\frac{1}{2}$  gr., powdered belladonna  $\frac{1}{10}$  gr., and caffeine  $\frac{1}{2}$  gr. In epilepsy, migraine and spasmodic affections.

[P1 81 84] **Cafinal (Bayer Products, London)** Tablets of Luminal  $\frac{1}{2}$  gr. and caffeine  $\frac{1}{2}$  gr. *Dose.*—1 to 3 tablets daily. In migraine, epilepsy, dysmenorrhœa, etc.

[P1 81 84] **Optinoktin (Richter, London)** Phenobarbitone 0·1 g., bromosulvalerylurea 0·2 g., amidopyrine 0·2 g. *Dose*—1 or 2 tablets nightly. Neuralgia, migraine, etc.

[P1 81 84] **Salepsal (Coates & Cooper, London)** Phenobarbitone 0·05 g., *Rhamnus Purshiana* 0·1 g., antispasmodic vegetable extracts (datuna, scopolia, valerian) *Dose*—1 to 6 pills per day. For epilepsy.

[P1 81 84] **Phenobarbitonum Solubile (B.P., P.G. VI, P. Helv. V,**

*P. Svec. X, P. Dan.*). *Syn.* SODIUM PHENOBARBITONE, SOLUBLE PHENOBARBITAL (*U.S.P. XI*), GARDENAL-SODIUM (*Pharmaceutical Specialities (May & Baker) Ltd., London*), LUMINAL-SODIUM (*Bayer Products, London*).  $C_{12}H_{11}O_3N_2Na = 254.1$ .

*Dose.*— $\frac{1}{2}$  to 2 grains (0.03 to 0.12 g.). It has also been given hypodermically in doses of  $\frac{1}{2}$  to 3 grains (0.03 to 0.2 g.) daily in 20% solution, e.g., in epilepsy, but the matter is *sub judice*. *P.G. VI* states max. single dose 6 grains, max. daily dose 12 grains; *P. Helv. V* has 3 and 5 grains approx. respectively.

It is the mono-sodium derivative, and occurs as a white hygroscopic powder with bitter taste. *Soluble* readily in cold water and in alcohol 90%; insoluble in ether or chloroform. Aqueous solutions should be freshly prepared with recently boiled and cooled water.

**Incompatible** with ammonium salts as they decompose quickly, also with acids and acidic substances which precipitate phenobarbitone. In preference give it alone. Solutions should not be heated, since phenylethylacetylurea is precipitated. The same decomposition may occur on long standing.

**DECOMPOSITION IN AQUEOUS SOLUTION.** Soluble phenobarbitone slowly hydrolyses in solution with production of  $CO_2$  and a precipitate of phenylethylacetylurea. A 10% solution (pH 9.4) decomposes only to the extent of 1% at 20° in three weeks. The more strongly alkaline solutions decompose somewhat more rapidly than those containing less alkali.—*L. Nielsen, Dansk Tidsskr. Farm., 1933, 7, 137*

**PHENOBARBITONE SOLUTION FOR INJECTION.** The instability and alkalinity of solutions of soluble phenobarbitone make it unsuitable for injection. The following solution has been found satisfactory.—Phenobarbitone 20 g, amylene hydrate 38 g., ethyl urethane 35 g., water 7 ml. Sterilise by filtration using pressure rather than suction in order to avoid evaporation.—*E. V. Christensen, Arch. Pharm. Chem., 1932, 89, 529.*

**Toxic Effects of Phenobarbitone.** Scarlatinaform rashes produced by Luminal 1 grain *bis die*.—*I. Sachs, Brit med. J., ii/1925, 1098.*

Eruption resembling measles following use of 0.1 g of Luminal-Sodium daily for 11 days.—*Per J. Amer. med. Ass., ii/1925, 707*

Dermatitis, with total loss of hair and nails, following daily administration for three weeks of 0.1 g. of Luminal.—*Brit med J Epit, ii/1924, 53. See also J. Amer. med. Ass., i/1922, 1199, Prescriber, 1923, 23*

A case of Luminal poisoning.—*Lancet, ii/1925, 596.*

It has generally been found that the effective dose of Luminal is very near the toxic dose, more than 3 grains daily producing ataxia.—*J. H. Hannan, Practitioner, ii/1927, 262.*

Luminal rash, 41 cases. It seems that the cause must be a selective tissue reaction to the drug dependent on constitutional factors about which we are still ignorant.—*W. C. Menninger, J. Amer. med. Ass., ii/1928, 18*

Of 11 cases of attempted barbiturate suicide seen in Lille during 1934, 8 were due to phenobarbitone and 3 were fatal. The doses taken ranged from 1.7 to 7 g. One person survived 5 g. and the two lethal doses ascertained were 6 and 7 g. The treatment adopted was a combination of strychnine, Coramine and alcohol.—*Carrière and Huriez, Pr. méd., 1935, 465.*

*For treatment of phenobarbitone poisoning, see Antidotes to Barbiturate Poisoning, p. 255.*

#### References.

**EPILEPSY.** In major type of fits useful, but is of no value in hysterical fits. Tolerance is apt to occur, so that the results in the first 3 months may be the best. Outside a resident institution, 3 to 4 grains should be made the maximum dose in 24 hours.—*Lancet, ii/1926, 713. See also ibid., 728, 840, 892, 943.*

Status epilepticus well treated by hypodermic injection of Luminal-Sodium from  $\frac{1}{2}$  to 3 gr. Solution should be freshly prepared—W. J. T. Kimber, *Brit. med. J.*, i/1926, 16.

Some striking results stopping its use followed by an increase of fits.—J. Tylor Fox, *Lancet*, ii/1927, 589. See also W. Johnson, *ibid.*, 733.

Epilepsy treated by Luminal Doubtful whether 5 or 6 grains should be exceeded as a single dose *per os* Rashes and poisoning symptoms—headaches, vertigo, lethargy, etc. Also of use in migraine, insomnia (1 to  $1\frac{1}{2}$  grain at bedtime), aural vertigo Recurrent attacks well treated. Also in cutaneous affections with a neurotic factor—W. Russell Brain, *Lancet*, ii/1929, 867.

At the David Lewis Colony, treatment is instituted with 2 gr. of soluble phenobarbitone dissolved in  $\frac{1}{2}$  oz. of water and given each morning At the end of 2 weeks any nausea or sleeplessness should have disappeared The case is reviewed at the end of a month and appropriate alterations made (*e.g.*, alteration of dose, time of giving, etc.) The drug may be stopped at the end of 6 months if no change has been produced or is expected. Administration is safe over long periods. In 1933 over 400 patients were taking the drug regularly some had taken it daily for more than 12 years No knowledge of a single case of phenobarbitone addiction in an epileptic, and no instance of Luminal skin rash has been observed—R. Handley, *J. ment Sci.*, 1934, 80, 526.

HYPERTENSION. Arterial blood-pressure in 85% of cases of hypertension, decreased by phenobarbital. Large doses produce marked toxic symptoms.—Per J. Amer. med. Ass., ii/1925, 1427

MIGRAINE. Bromide failed in migraine, and in a few cases aspirin, and in others Pyramidon 7 gr. with cannabin tannate 3 gr., cut short the duration of the headache. True migraine, which in its characteristic type, is notably hereditary, has been treated with best success by Luminal. The dose, as a rule, should not be more than  $\frac{1}{2}$  gr. thrice daily at first, reduced to twice daily after a fortnight if the result is good, and later to once daily at bedtime After a week various cutaneous rashes may be seen, but are unlikely if the above dosage is not exceeded—Wilfred Harris, *Brit. med. J.*, ii/1922, 786. See also R. Hearn, *Brit. med. J.*, ii/1922, 893.

PAINFUL CONDITIONS. Hypodermic injection of  $1\frac{1}{2}$  grains effective in severe pain, such as tabetic crises and herpes zoster. Relief in 20 to 30 minutes—L. Gunther and H. M. F. Behneman, per J. Amer. med. Ass., ii/1928, 832.

VOMITING OF PREGNANCY completely controlled by  $\frac{1}{2}$  to 1 grain of Luminal nightly, but tends to recur if drug is omitted. Non-toxic in this dose over long periods.—A. Elliott, *Brit. med. J.*, ii/1931, 1119.

[P1-S1-S4] *Mistura Phenobarbitoni* (*Gt. Orm. H.*). (Dose for 1 year old child). Soluble phenobarbitone  $\frac{1}{2}$  gr., potassium bromide 2 gr., elixir of gluside  $\frac{1}{2}$  m., chloroform water to 1 dr.

[P1-S1-S4] *Tabellæ Phenobarbitoni Solubilis* (*B.P.C.*) Contain  $\frac{1}{2}$  gr. (0.03 g.)

[P1-S1-S4] *Lubrokai* (*Braun, London*). Tablets of potassium bromide and soluble phenobarbitone Dose.—1 tablet 3 times daily. Convulsions and nervous insomnia.

[P1-S1-S4] *Prominal* (*Bayer Products, London*). *N*-Methylethylphenylmalonylurea. Dose.—0.2 to 0.4 g. daily. Anti-epileptic and anti-spasmodic without hypnotic action.

EPILEPSY.—Led to a striking reduction in the incidence of fits in 10 cases and patients were more bright, cheerful and contented. In four cases Prominal was substituted for Luminal with improved results. The usual dose was 3 grains once or twice daily. A daily dose showed no cumulative effect.—L. G. M. Page, *Brit. med. J.*, i/1936, 531. Results corroborated in four cases.—L. Barber, *ibid.*, 666.

[P1-S1-S4] *Rutonal* (*Pharmaceutical Specialties (May & Baker) Ltd., London*). Methylphenobarbitone.

Dose.—On the first day one 3-grain tablet in the morning and one at night to test the patient's tolerance, increasing to 4 or 5 tablets in 24 hours. Hypnotic and sedative; specially indicated in epilepsy.

[P1-S1-S4] *Allobarbitonum* (*B.P.C.*). *Syn. and Prop. Name.* ALLOBARBITALUM (*P. Helv. V.*), DIAL (*Ciba, London*) ( $1\frac{1}{2}$  gr. tablets), 5 : 5-DIALLYLBARBITURIC ACID, DIALLYLMALONYUREA.



**Dose.**— $\frac{1}{2}$  to 3 grains (0.03 to 0.18 g.). *P. Helv. V* has max. single dose 3 grains, max. in 24 hours 5 grains.

A white, odourless, crystalline powder with a slightly bitter taste. M.p.  $171^\circ$  to  $172^\circ$ . Prepared by the condensation of ethyl diallylmalonate with urea.

**Soluble** in alcohol and ether, and in alkaline solutions; slightly soluble in water.

**Uses.** A hypnotic more readily absorbed than barbitone. Idiosyncrasy, with a rash and fever, may occur.

Recovery after taking 2.7 g. of Dial—*Brit. med. J. Epit.*, 11/1927, 103.

[P1 81 84] **Cibalgin** (*Ciba, London*).

A compound of amidopyrine with Dial (0.25 g. = 0.22 g. of amidopyrine and 0.03 g. of Dial).

Tablets 4 grains (0.25 g.). **Dose** 1 to 4. Liquid for oral use, 1 ml. = 0.25 g. (4 grains) Cibalgin. **Dose**  $\frac{1}{2}$  to 4 ml. Ampoules each containing 2.3 ml. Cibalgin (1 ml. = 0.25 g.) **Dose**  $\frac{1}{2}$  or 1 ampoule daily. The tablets and liquid should be taken with a little warm water or tea, but not in coffee. In neuralgia, migraine, and other types of pain, e.g., dysmenorrhœa, articular and muscular pain.

[P1 81 84] **Dialacetin** (*Ciba, London*) Tablets contain 4 gr. of allyl-*p*-acetamino-phenol and  $1\frac{1}{2}$  gr. of Dial. For use as combined hypnotic, analgesic and antipyretic. **Dose**—As hypnotic, 1 to 2 tablets with hot drink one hour before bedtime. As sedative,  $\frac{1}{2}$  to 1 tablet one to three times a day.

Nocturnal fits in epilepsy often respond to this ( $\frac{1}{2}$  to 1 tablet at night, or twice daily) when other remedies fail.—C. Worster-Drought, *Lancet*, 11/1925, 892, 1095.

[P1 81 84] **Didial** (*Ciba, London*) Tablets contain  $\frac{1}{2}$  grain of diallylbarbiturate of ethylmorphine, and  $1\frac{1}{2}$  grains of Dial, equivalent to  $\frac{1}{2}$  gr. of ethylmorphine and  $1\frac{1}{2}$  gr. of Dial. A powerful hypnotic for severe insomnia. **Dose**—1 tablet. For the induction of "twilight sleep," one to three tablets.

[P1 81 84] **Hemypnone** (*Ciba, London*) Ethylmorphine diallylbarbiturate and chlorbutol. Tablets contain  $\frac{1}{2}$  gr. of the former and  $7\frac{1}{2}$  gr. of the latter, and suppositories  $\frac{1}{2}$  and  $9\frac{1}{2}$  gr. respectively. For the induction of "twilight sleep."

[P1 81 84] **Somnifaine** (*Hoffmann-La Roche, London*). A water-glycerin-alcohol solution of the diethylamine salts of diethylbarbituric acid (barbitone) and allylisopropylbarbituric acid, containing the equivalent of 0.1 g. (about  $1\frac{1}{2}$  gr.) of each acid per ml. Available as a flavoured oral solution in drop bottles or in ampoules for injection.

**Dose.**—Orally, 20 to 40 drops (about 8 to 16 m.) 30 minutes before retiring; may be increased up to 60 drops (25 m.). To be taken in water or other vehicle. By injection, 1 ampoule (2 ml.) intramuscularly. In case of urgency, 2 to 3 ampoules by very slow intravenous injection. A powerful sedative and hypnotic indicated in all conditions of excitement, ravings, or convulsions, in eclampsia, status epilepticus, tetanus, strychnine and cocaine poisoning. Also used in the "twilight sleep" treatment of certain mental disorders.

**PSYCHOSES.**—Treatment of psychoses by prolonged narcosis—intramuscular injection of Somnifaine in 2 ml. doses, sufficient to ensure continuous sleep for 10 to 12 days, feeding with fluids being carried out before each injection and at intervals when possible; largest daily dose usually 8 ml. The treatment is dangerous (3 deaths in 60 cases) but often produces definite, and sometimes dramatic, improvement. The concurrent administration of insulin with glucose made for smoother treatment.—D. N. Parfitt, *Lancet*, i/1936 424.

As this high mortality rate (5%) might well dissuade others from carrying out this valuable form of treatment it should be pointed out that it is not in accord with experience at Cardiff City Mental Hospital. When Somnifaine alone was used there were 2 deaths in 86 treatments (2.3%), but since glucose and insulin have been used to combat toxic symptoms 154 cases have been treated without a single fatality. With careful nursing in a darkened single room, it is rarely found necessary to give more than 4 ml. of Somnifaine in the 24 hours—P. K. McCowan, *Lancet*, 1/1936, 508.

**STATUS EPILEPTICUS.**—Somnifaine intramuscularly advocated as an efficient remedy. Lumbar puncture and free drainage of spinal fluid, with Sodium Luminal, 6 grains intravenously, also recommended as immediate measures for checking seizures. A 50% solution of magnesium sulphate *per os* cleans alimentary tract and reduces intracranial pressure—F. McLaughlin, *Practitioner*, 11/1932, 714.

[P1 81 84] **Allonal** (*Hoffmann-La Roche, London*). A combination of allylisopropylbarbiturate of amidopyrine 0.126 g. (approx. 2 gr.) and amidopyrine 0.034 g. (approx.  $\frac{1}{2}$  gr.), equivalent to about 1 gr. of allylisopropylbarbituric acid and 1  $\frac{1}{2}$  gr. of amidopyrine.

**Dose.**—1 to 2 tablets as sedative or hypnotic in simple cases of insomnia, 2 to 4 as analgesic and hypnotic.

2 tablets quickly relieve pain in neuralgia, neuritis, rheumatism, sciatica, etc. Is not habit-forming, and has low toxicity. *Not more than 4 or 5 tablets daily advised until patient's susceptibility is ascertained*.

Death of a woman who had taken 10 tablets a day for more than a year.—*Pharm. J.*, 1/1932, 117, 139.

[P1 81 84] **Pernocton** (*Riedel-de-Haen, Berlin; Old Strand Chemical Co., London*). SODIUM BUTYL- $\beta$ -BROMALLYL-BARBITURATE.  $C_{11}H_{14}O_3N_2BrNa = 325.0$ .

Issued in ampoules containing 3  $\frac{1}{2}$  grains in 2.2 ml. Average hypnotic dose intravenously 3 ml. (containing 4  $\frac{1}{2}$  grains), given at the rate of 1 ml per minute.

Resembles Sodium Amytal in action, but is a more powerful hypnotic. In addition, there is less restlessness during recovery period. No fall in blood pressure. The solution is ready for use.—E. I. McKesson and K. C. McCarthy, *Brit. med. J.*, 11/1930, 902.

Pernocton advocated—E. I. McKesson, *Lancet*, 11/1930, 797.

**DENTAL WORK.**—Pernocton intravenously. A good anæsthetic, conducting operation under gas and oxygen through a Magill tube. Nembutal and Avertin also suitable, but no advantage over Pernocton.—R. R. Macintosh, *Brit. dent. J.*, Feb. 15, 1932.

**MORPHINISM.**—A cure obtained in from 4 to 5 days, in the patient's own home, in all but one of 12 cases. Twilight sleep is induced during this period by three injections at 8 a.m., 4 p.m. and midnight, Pernocton 2 ml. intravenously and 2.2 ml. intramuscularly being injected thrice daily. To the intramuscular injection is added 0.002 g. of atropine to obviate the disorders of abstinence. Food in fluid form given prior to each injection, and fruit juice and glucose in between.—L. König, *Med. Klinik*, 1935, 246.

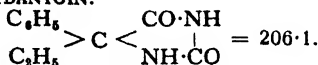
[P1 81 84] **Sandoptal** (*Sandoz, London, Brooks & Warburton, London*). *iso*Butylallylbarbituric acid. Tablets contain 3 grains. **Dose.**—In simple insomnia 1 tablet; in persistent insomnia 2 tablets.

[P1 81 84] **Optalidon** (*Sandoz, London, Brooks & Warburton, London*). Sandoptal 0.05 g., amidopyrine 0.125 g., caffeine 0.025 g. **Dose.**—2 tablets several times daily as required. Sedative and hypnotic.

[P1 81 84] **Noctal** (*Riedel-de-Haen, Berlin; Old Strand Chemical Co., London*). *iso*Propylbromopropanylbarbituric acid. **Dose.**—1 or 2 tablets before retiring. Narcotic and sedative.



[P1·81·87] **Nirvanol** (Heyden, Dresden; Braun, London).  $\gamma\gamma$ -PHENYLETHYLHYDANTOIN.



[P1] "*Phenylethylhydantoin; its salts, its acyl derivatives; their salts.*"

[81] "*Phenylethylhydantoin; its salts; its acyl derivatives; their salts.*"

[87] *Medicines made up ready for the internal treatment of human ailments containing phenylethylhydantoin, its salts; its acyl derivatives; their salts, must be labelled with the words "Caution. It is dangerous to take this preparation except under medical supervision" instead of the word "Poison"*

Formed by combination of urea and glycol. A tasteless crystalline powder, slightly soluble in water. Hypnotic and sedative. Not to be administered over lengthy periods.

*Dose.*—In chorea, the usual daily dose is 0·2 g. to 0·5 g. spread over 2 or 3 doses.

Treatment stopped on appearance of exanthema, or increase in temperature. It must only be given under most careful observation.

In chorea, 0·3 g. *per os* daily for a child of 9 to 14 years. In most cases 8 to 14 days after beginning of treatment there is a well marked morbiliform rash accompanied by pyrexia. The drug is then stopped. It causes a change in the blood, viz., a true eosinophilia reaching its maximum just before appearance of the rash. In addition there is generally a leucopenia. Conjunctivitis and œdema of the eyelids should be watched for and treatment stopped immediately. Report of 6 cases with beneficial results. Originally advocated as hypnotic, and as a sedative in epilepsy and various types of psychoses—F. J. Poynton and B. Schlesinger, *Lancet*, ii/1929, 267.

0·25 g. from 5 to 9 years, half of which is given twice a day 0·3 g. given in two doses never exceeded. The aim is to produce a reaction and stop, and in any case it is stopped in 14 days.—F. J. Poynton, *Index of Treatment*, 1931.

Symptoms improved and attack sometimes cut short in a dramatic way. Only to be used under constant supervision—C. F. T. East and E. R. Cullinan, *Lancet*, ii/1930, 190.

After-results disappointing. Only exploitation of a new sedative whose super-excellence has yet to be proved. Doubtful whether it will outlive the popularity due to its novelty. Adalin preferable.—R. Miller, *Med. Annu.*, 99.

Purpura hæmorrhagica, nephritis, and a fatal case of dermatitis exfoliativa have followed its use in chorea. Effective, but catastrophe can neither be seen, foreseen nor prevented.—*Lancet*, ii/1931, 545.

No permanent benefit in three obstinate cases of chorea, and one patient suffered a dangerous reaction.—T. D. Jones and J. L. Jacobs, *J. Amer. med. Ass.*, ii/1932, 21.

Only used in severe and stubborn cases. The chief danger is temporary mental derangement and it is not advisable to give it to a mentally deficient child. The drug is stopped when the rash and large glands appear or if there is no reaction on the twelfth day. It is a drug that needs discretion but has been found very serviceable.—*Per Brit. med. J.*, i/1933, 903.

## BARIUM

Ba = 137·36.

[P1] "*Barium, salts of, other than barium sulphate and the salts of barium specified in Part II of this List.*"

[P2] "*Barium, salts of, the following:—Barium carbonate, barium silicofluoride.*"

[81] "*Barium, salts of.*"

[86] "*Barium, salts of—specify proportion as the proportion of one particular barium salt which the preparation would be calculated to contain on the assumption that the barium (Ba) in the poison had been wholly converted into that salt.*"

Rule 10 of the Poisons Rules, 1935, exempts from the application of the Pharmacy and Poisons Act, 1933, and of the Rules made under that Act, all articles containing barium carbonate and prepared for the destruction of rats and mice.

[P1 81] **Barii Chloridum.** Syn. BARIUM CHLORATUM (P.G. VI).  $\text{BaCl}_2, 2\text{H}_2\text{O}$

Dose.— $\frac{1}{2}$  to 2 grains (0.03 to 0.12 g.). P.G. VI max single dose 3 grains; or 9 grains *per diem*.

Colourless crystalline plates, with bitter saline taste. **Soluble** 1 in  $2\frac{1}{2}$  of water. Solution is destructive to bacteria. **Incompatible** with sulphates, phosphates, tartrates and carbonates.

**Antidotes.** Empty stomach by emetic or by stomach tube, using 2 oz. of magnesium sulphate in 2 gallons of water. Give 1-oz. doses of sodium or magnesium sulphate, well diluted, and repeated if necessary. Keep patient warm and give demulcent drinks. Stimulants for collapse.

Mostly used for analytical purposes, but is of value as a heart tonic, resembling digitalis in action. Raises blood pressure by constriction of vessels. 1% solution has been used as eye-wash in scrofulous inflammation.

Barium chloride, 0.03 g., three or four times daily by the mouth is sometimes of value in Stokes-Adams attacks—*Lancet*, 1/1927, 401

Difficult to credit barium chloride with the power of preventing Stokes-Adams seizures—A R Gilchrist, *Brit. med. J.*, 1/1934, 613

Typhoid has been treated with barium chloride *per os* with good results in 33 out of 35 cases. Dose.—1 to  $1\frac{1}{2}$  grains, increased progressively to 7 $\frac{1}{2}$  grains thrice daily for 6 to 7 days with intervals of 3 to 5 days—*Prescriber*, 1929, 224. No bad results except vomiting 1.5 g each day in divided doses for 5 days, with 5-day interval, then repeated for further 5 days.—E. Petrina, *Brit. med. J. Epit.*, 1/1931, 96.

**Barii Sulphas** (B.P., P.G. VI, U.S.P. XI, F.E. VIII, P. Ital. V, P. Helv. V, P. Dan., P. Belg. IV)  $\text{BaSO}_4 = 233.4$ .

Dose.—For X-ray work only, 2 to 5 ounces (60 to 150 g. approx.) in a cornflour or other "meal" of about 6 to 15 ounces.

A white powder insoluble in water and acids.

For outlining portions of the alimentary tract, instead of bismuth carbonate and subnitrate (q.v.).

Barium sulphate suspensions in olive oil 10, 20%, etc., have been used for bladder examination.

[P1-81] **Barium Thiosulphate** inadvertently administered in place of barium sulphate caused death.—*Pharm. J.*, 11/1921, 315.

**Caution.**—*Barium carbonate* is also soluble and hence poisonous. Confusion with bismuth carbonate occurred.—*Pharm. J.*, 11/1921, 344.

**Sulfate de Barium Gelatineux** (*Fr. Cx. Supp.*, 1926) is in paste form, containing 55 to 58% of water.

**Pulvis Barii Sulphatis Compositus (B.P.C.).** *Syn* BARIUM MEAL, SHADOW MEAL.

Contains 75% of barium sulphate in a cocoa-flavoured powder.

*Dose.*—4 to 8 ounces (120 to 240 g.) mixed immediately before use with sufficient boiling water poured directly on to the powder.

*Gt. Orm. H.* is similar, containing dried milk instead of arrowroot.

**Emulsio Barii (Brompton H.).** Barium sulphate 4 oz, tragacanth 40 gr, water to 12 oz.

**Emulsio Barii Sulphatis (C X H).** Barium sulphate 10 oz, essence of raspberry 60 m, soluble saccharin 1 gr, mucilage of tragacanth to 20 oz

*R I Edin.* has barium sulphate 1 oz, sugar half a teaspoonful, oatflour 2 teaspoonfuls, suspended in milk. This is given at 5 a.m. on the day of examination. At 10 a.m., shortly after the first series of radiographs has been taken, a second meal is given consisting of barium sulphate 4 oz, mucilage of acacia q.s, water to 10 oz.

*St. Mark's H.* has barium sulphate 5 oz, tragacanth 45 gr, alcohol 90% 30 m, elixir of saccharin, vanillin  $\frac{1}{2}$  gr, water to 10 oz

*U.C.H.* has barium sulphate 10 oz, mucilage of starch q.s, vanillin  $\frac{1}{2}$  gr, saccharin  $\frac{1}{2}$  gr., alcohol 90% 1 dr, chloroform 5 m, water to 1 pint (For average dose.)

**Enema Barii Sulphatis (C L H).** Barium sulphate 8 oz, mucilage of tragacanth to 20 oz. *U C H.* has barium sulphate 40 oz, tragacanth powder 1 dr., water to 80 oz.

**Albarol (Pharmaceutical Specialities (May & Baker) Ltd, London)** A barium meal containing 90% of barium sulphate. Administered orally, the contents of a box being mixed with water to form a cream

**Barium Meal G.L. (Glaxo Laboratories, London)** contains barium sulphate 100, milk solids and chocolate 47, suspending agent 3

**Barolac (Burroughs Wellcome, London)** A 30% suspension of finely divided barium sulphate containing no mucilaginous suspending agent

**Citobaryum (Merck, Darmstadt, Martindale, London)** Barium sulphate meal. 150 g is made into a paste with 200 ml. of water.

**Fotamilko, Fotamealo and Fotonemal (Evans, Sons, Lescher & Webb, Liverpool)** Barium sulphate meals, the first is a thin, lemon-flavoured fluid, the second is a thick cream containing tragacanth and flavoured with cocoa and sugar, and the third forms a simple, lemon-flavoured suspension

**Neobar (Merck, Darmstadt, Martindale, London)** Barium sulphate meal supplied in 150 g. packets to which water (up to 300 or 350 ml) is added to form a paste or liquid.

**Nov-Umbrose (Allen & Hanburys, London)** Ready-mixed barium meal containing 75% of barium sulphate. Also supplied as a cream (a 1 in 1 preparation) **Umbrose** is a similar preparation.

**Shadoform (British Drug Houses, London).** Flavoured barium sulphate powder. **Shado-cream** A 50% suspension ready for use.

[P1 81] **Baryta Sulphurata (B.P.C.).** *Syn* BARIUM SULPHIDUM. BaS = 169.4.

*Dose.*— $\frac{1}{2}$  to 1 grain in pills coated so as to be more likely to dissolve in the intestines than in the stomach.

A greyish yellow powder, partially soluble in water, the solution decomposing slowly with loss of hydrogen sulphide. Has been given as an alternative in syphilitic affections, but its main use is as a depilatory.

[P1 81] **Barium Sulphide Depilatory.** *Syn* CAUSTICUM BARIUM.

Barium sulphide, in fine powder from 1 to 3, wheat starch 3.

When required for use, make into a cream with water, spread

on the part and let it remain five or ten minutes, then remove with a blunt knife. It temporarily reddens the skin.

[P1 81] *Another formula* is barium sulphide 5, powdered soap 1, French chalk 7, starch 7. One part of this mixed with 3 of water is applied and, to avoid possible dermatitis, is washed off after 5 minutes. May be used from time to time.

**Strontium Sulphide**,  $\text{SrS} = 119.7$ , is also used. A patented German preparation contains strontium sulphide 12, corn starch 40, talc 35, dextrin 7, nerolin 1, and essential oil 5 parts. It is claimed that the dextrin protects the skin and hair papilli and prevents the bad odour during use.—*Pharm. J.*, 1/1925, 13.

## BELLADONNA

*Syn* DEADLY NIGHTSHADE.

[P1] "*Alkaloids, the following; their salts, simple or complex:—Belladonna, alkaloids of.*"

[81] "*Alkaloids, the following, their salts, simple or complex:—Belladonna, alkaloids of, except substances containing less than 0.15% of the alkaloids of belladonna calculated as hyoscyamine.*"

[86] "*Alkaloids—Belladonna, alkaloids of—specify proportion as the proportion of any one alkaloid of belladonna that the preparation would be calculated to contain on the assumption that all the alkaloids of belladonna in the preparation were that alkaloid.*"

By Rule 10 of the Poisons Rules, 1935, machine-spread plasters are exempt from the provisions applying solely to substances in the First Schedule to the Rules.

All parts of the plant *Atropa Belladonna* (Solanaceæ) yield the alkaloids hyoscyamine and atropine. The root contains from 0.3 to 0.8% (Maben states rarely as much as 0.5%) of total alkaloids—chiefly hyoscyamine. Doubtful whether any atropine is present. Dried leaves of good quality contain 0.4 to 1%, principally hyoscyamine.

**Antidotes.** Treat as for poisoning by atropine, see p. 228.

[P1 81] **Belladonnæ Folium** (B.P., U.S.P. XI, F.E. VIII, P. Belg. IV (as Belladonnæ Pulvis), and P. Helv. V) contain not less than 0.3% of total or mydriatic alkaloids calculated as hyoscyamine.

*Dose.*— $\frac{1}{2}$  to 3 grains (0.03 to 0.2 g.).

The leaves of *Fr. Cx.* and *P. Dan.* have no standard. Maximum single dose 2 grains, maximum during 24 hours  $7\frac{1}{2}$  grains approximately. *P. Ital. V.* not standardised, approximately  $1\frac{1}{2}$  and 6 grains respectively.

**Uses.** To check action of secretory glands. Powerful antispasmodic in intestinal colic, spasmodic asthma and bladder spasm due to calculi or prostatic irritation. Full doses of extract or tincture are useful in whooping cough and false croup, also in enuresis, hyperacidity being corrected by potassium citrate or

excessive alkalinity by sodium acid phosphate. Broncho-pneumonia is sometimes well treated in the early stages by 4 to 5 m. doses of tincture or  $\frac{1}{4}$  gr. of extract every 3 to 4 hours, combined with diuretics and diaphoretics. In dyspepsia, belladonna reduces gastric secretion and inhibits spasmodic contractions. Large doses of tincture or extract are of value in post-encephalitic parkinsonism.

URINARY INCONTINENCE. Belladonna should only be used to "break the habit" and never pushed for more than two months at a time. It is useless and even harmful when there is definite lack of tone in the sphincters; here nux vomica is indicated. Thyroid (advocated by Leonard Williams) is useful in some cases, especially when there are adenoids. Alkalis may be useful where the urine can be shown to be hyperacid—F. Hernaman-Johnson, *Lancet*, 1/1921, 1295

[P1-81] **Belladonna Pulverata (B.P.).** *Syn* PULVIS BELLADONNÆ

*Dose.*— $\frac{1}{2}$  to 3 gr. (0.03 to 0.2 g.).

Consists of belladonna leaf in fine powder adjusted with exhausted belladonna leaf to contain 0.3% of alkaloids calculated as hyoscyamine. It is officially required to be dispensed when *Belladonnæ Folia* is prescribed.

[P1] **Collyrium Belladonnæ (B.P.C.).** Green extract of belladonna 0.5% *w/v*.

[P1] **Collyrium Belladonnæ Compositum (K C H)**

Boric acid 15 gr., quinine hydrochloride  $7\frac{1}{2}$  gr., liquid extract of belladonna 10 m., distilled water to 1 oz.

[P1-81] **Emplastrum Belladonnæ Viride (B.P.C.).**

Contains dry extract of belladonna equivalent to 0.25% of alkaloids in rubber adhesive plaster.

[P1-81] *Fr. Cx.* has belladonna extract (*Fr. Cx. q.v.*) 1, elemi 1, diachylon plaster (*Fr. Cx.*) 2.

[P1-81] **Extractum Belladonnæ Siccum (B P)** *Syn* EXTRACTUM BELLADONNÆ ALCOHOLICUM.

*Dose.*— $\frac{1}{4}$  to 1 grain (0.016 to 0.06 g.).

This is prepared from the leaf—it is a mixture of alcoholic extract and powdered leaf, containing 1% of alkaloids. The more powdered leaf present in the extract the better it keeps. *I.A.*, 1930, recommended 1.3% alkaloids. *P Ital V* is 1% total alkaloids, made by means of 95% alcohol.

[P1-81] **Extractum Belladonnæ (U.S.P. XI).**

*Average dose.*— $\frac{1}{4}$  grain (0.015 g.).

Two forms, pilular extract and powdered extract are official. They are of approximately the same strength as *Extractum Belladonnæ I.A.*, i.e. 1.25% of alkaloids.

[P1-81] **Extractum Belladonnæ (I.A.)** to be a "solid" extract (containing about 10% of water) prepared by means of alcohol 70% from the leaf. *Fr. Cx.* and *P. Dan.* agree with *I.A.* The *Fr. Cx.* follows the *I.A.* method of making and gives a method of assay, but does not set up a standard. It states max. single dose  $\frac{1}{4}$  grain; max. in 24 hours  $1\frac{1}{2}$  grains approx. *P. Ital. V* is similar, containing 1.25% of alkaloids. *P. Austr.*, is alcoholic from the leaves and contains 2% of alkaloids; [P1-81] *P. Ned. V* is the same but contains not less than 1.15 to 1.3% of alkaloids. [P1-81] *P. Belg. IV* contains 1.5% of alkaloids.

[P1-81] **Extractum Belladonnæ Viride (B.P.C.).**

*Dose.*— $\frac{1}{4}$  to 1 grain (0.016 to 0.06 g.).

A soft extract standardised to 1% w/v of alkaloids. It replaces the unstandardised extract of the *B.P.* '98 which was prepared from the juice of the fresh plant, and contained from 0.5 to 2% of alkaloids.

[P1 81] **Glycerinum Belladonnæ** (*B.P.C.*)

Green extract of belladonna 50% w/w with boiling distilled water, and glycerin.

To check pain and inflammation, is often painted on boils, abscesses and carbuncles, and covered with a poultice; also applied on lint to the breasts to disperse milk.

[P1] **Linctus Belladonna** (*T.H.*) *Dose*—1 drachm (4 ml)

Tincture of belladonna 24 m, bismuth carbonate 24 gr, tincture of lemon 80 m, glycerin 80 m, water to 1 oz.

[P1] **Mist. Bellad.** (*N.I.F.*)

Potassium iodide 3 gr, tincture of ipecacuanha 10 m, tincture of belladonna 5 m, arsenical solution 2 m, chloroform water to  $\frac{1}{2}$  oz.

[P1] **Mistura Belladonnæ Xanthoxyli et Hyoscyami.** *Syn* TOWNS'

**SPECIFIC.** *Dose*—6 to 8 minims (0.4 to 0.5 ml)

Belladonna leaf tincture (*U.S.P.* 1890) 2, fluidextract of xanthoxylum 1, fluidextract of hyoscyamus 1

The above dose is equivalent to a little less than 5 minims of *B.P.* tincture of belladonna. Said to be specific in morphinism, cocaineism and alcoholism.

Increase from 6 drops, by 2 drops every 6 hours, until 16 drops have been reached. Discontinue for a few doses if symptoms of belladonna poisoning are observed.—E. Huntington Williams, "Opiate Addiction"

[P1 81] **Pilula Belladonnæ, Nucis Vomice et Cannabis.**

Extracts of belladonna, nux vomica and cannabis, of each  $\frac{1}{2}$  gr. For the constipation in gastric ulcer. The cannabis has a good effect on the mental side, belladonna regulates peristalsis and the nux vomica has a good effect as an aperient and for improving tone of the gut.

[P1] **Tinctura Belladonnæ** (*B.P., I.A.*)

*Dose.*—5 to 30 minims (0.3 to 2 ml.).

Prepared with about 10% of dried leaf, and standardised to contain 0.03% of alkaloids. *Fr Cx., P Ital V, P Ned. V, and U.S.P. XI* are similar

A fatal case of (most probably) chronic belladonna poisoning, in which  $\frac{1}{2}$  to 2 drachms of the tincture had been taken every day for 6 years.—J. Spears, *Brit med. J.*, 1/1927, 1105.

POST-ENCEPHALITIC PARKINSONISM well treated with tincture of belladonna, 45 minims daily.—A. J. Hall, *Brit med J.*, 1/1926, 129

A man who had been taking  $1\frac{1}{2}$  dr. of tincture of belladonna daily for many months with considerable benefit, began to lose ground. Suddenly he showed great improvement, which could not be accounted for until he admitted he had been taking double doses of his medicine. Many patients now take as large or larger doses without any toxic symptoms.—A. J. Hall, *Lancet*, 1/1934, 595.

[P1 81] **Bellafoline** (*Sandoz, London; Brooks & Warburton, London*) Preparations containing the natural alkaloids of belladonna leaf: *l*-hyoscyamine is present in an invariable and constant proportion with the secondary belladonna alkaloids (hyoscyne, atropamine and belladonnine). Tablets contain  $\frac{1}{10}$  gr. total alkaloids; solution, 1 : 2000; 1 ml. ampoules =  $\frac{1}{10}$  gr.

[P1-81 84] **Belladonal Tablets** (*Sandoz, London, Brooks & Warburton, London*). Contain  $\frac{1}{10}$  gr. of Bellafoline and  $\frac{1}{2}$  gr. of phenobarbitone. In angina pectoris, migraine and epilepsy

[P1-81 84] **Bellergal Tablets** (*Sandoz, London; Brooks & Warburton, London*). Contain Bellafoline 0.0001 g., Femergin 0.0003 g., phenobarbitone 0.02 g. In diseases of the autonomic nervous system.

[P1] **Jocigares** (*Wilcox, Jozau, London*). Cigarettes containing extracts of belladonna, stramonium and digitalis. *Dose.*—4 to be smoked daily. For asthma and hay fever.

[P1 81-84] **Thalassan** (*Promonta, Hamburg; Pharmaceutical Products, London*). Tablets containing extracts of belladonna and nux vomica with diallylbarbituric acid. Preventive of sea, train and air-sickness. *Dose*.—1 or 2 tablets just before commencement of journey, repeated after 2 hours if necessary

[P1 81] **Belladonnæ Radix** (*B.P., U.S.P. XI, P. Helv. V*).

*Dose*.— $\frac{1}{2}$  to 2 gr. (0.03 to 0.12 g.).

Contains not less than 0.4% of alkaloids calculated as hyoscyamine. *U.S.P. XI* and *P. Helv. V* require 0.45% of total alkaloids of belladonna.

**Uses.** Is used for the same purposes as the leaf, but chiefly in preparations for external use.

Relieves the pain of rheumatism, neuralgia, lumbago, chordee, and local inflammations, as of the breast. Also applied in phlebitis and to relieve the pain due to adhesions following pleurisy

[P1 81] **Chloroformum Belladonnæ** (*B.P.C.*)

Contains the equivalent of 50% *v/v* of liquid extract of belladonna. Applied as a paint or on lint for neuralgia and rheumatism.

[P1 81] **Collodium Belladonnæ** (*B.P.C.*) *Syn* LIQUID BELLADONNA PLASTER.

Liquid extract of belladonna 50% *v/v* and camphor 1.5% *w/v* in a collodion basis. For application to joints, or where a plaster is unsuitable.

[P1 81] **Emplastrum Belladonnæ** (*B.P.*) (*cf.* Emp Plumbi)

Contains 0.25% of the alkaloids of belladonna root, the aqueous-alcoholic percolate being evaporated and incorporated in plaster of colophony.

Bee and wasp stings are well treated by belladonna plaster—if slight, left on short time; if severe (*e.g.*, entered vein), several days may be necessary—gives considerable relief. Probably good for mosquito stings also.

Must not be applied by the midwife to mothers too ill to feed their babies, where there is heart disease, on account of paralysing effect of atropine on the vagus, with consequent quickening of heart's action.—W. H. F. Oxley, *Brit med J.*, 1/1931, 7

[P1 81] **Emplastrum Belladonnæ** (*U.S.P. XI*)

A standardised spread plaster prepared with adhesive plaster and an extract of belladonna root.

[P1 81] **Extractum Belladonnæ Liquidum** (*B.P.*)

*Dose*.— $\frac{1}{4}$  to 1 minim (0.015 to 0.06 ml.).

Prepared from belladonna root by a percolation process, adjusting so that the extract contains 0.75% of alkaloids.

*P. Ital. V* contains 0.25% *w/w*.

[P1 81] **Fluidextractum Belladonnæ Radicis** (*U.S.P. XI*)

*Average dose*— $\frac{1}{4}$  minim (0.05 ml.) Contains about 0.45% of alkaloids and is therefore about two-thirds the strength of the *B.P.* liquid extract.

[P1 81] **Linimentum Belladonnæ** (*B.P.*).

Prepared from belladonna root by percolation with a mixture of alcohol 90% (or *I.M.S.*) and water, and adjusted to contain 0.375% *w/v* of alkaloids, 5% *w/v* of camphor being added. A useful sedative for neuralgia and rheumatism.

Sprinkled on impermeable piline relieves lumbago.

[P1 81] **Linimentum Belladonnæ cum Chloroformo** (B.P.C.).

Chloroform, 1 in 8, with liniment of belladonna.

[P1] **Suppositorium Belladonnæ** (B.P.).

Contains  $2\frac{1}{2}$  m. (0.15 ml) of liquid extract of belladonna in 1 g of theobroma oil, *i.e.*, 0.001 g of root alkaloids.

[P1] **Pessaries** (60 grains weight) may also be made containing the same or double the quantity of extract.

Unilateral convulsions have been produced by their use, together with dryness of throat and dilated pupils (special idiosyncrasy).

[D1 P1 81] **Suppositoria Belladonnæ**  $\frac{1}{2}$  grain, et **Morphinæ Hydrochloridi**  $\frac{1}{2}$  grain.

These possess a useful sedative effect, and are valuable in irritated and painful conditions of the rectum and prostate, and for chordee.

[P1 81] **Unguentum Belladonnæ** (B.P.C.).

Contains the equivalent of 80% *v/w* of liquid extract of belladonna, or 0.6% *w/w* of alkaloids, in a basis of wool fat and benzoinated lard.

Said to be too strong for general use and may cause unpleasant symptoms.

To lessen excessive secretion in nasal catarrh, this ointment has been employed diluted 5 to 10 times with soft petroleum and a small proportion of tannin or gallic acid added.

[P1] **Unguentum Belladonnæ** (U.S.P. XI)

Contains about 0.125% of belladonna alkaloids, and is prepared with 10 parts of pulular extract of belladonna rubbed down with 5 parts of diluted alcohol and incorporated with a melted mixture of wool fat 5, yellow wax 5, and petrolatum 75.

[P1] **Unguentum Populi** (P. Belg. IV). Macerate dry belladonna leaves 125, dry henbane leaves 125 and dry poplar buds 200 (all bruised) in alcohol 90% 150 for 2 hours, warm on a water-bath with lard 1000 for 3 hours, stirring until the alcohol has evaporated. Strain, press and stir until the ointment sets.

The formula in *Fr. Cx.* differs from this.

**Zanthoxylum** (B.P.C.). *Syn.* XANTHOXYLUM, PRICKLY ASH BARK, TOOTHACHE BARK.

*Dose.*— $\frac{1}{4}$  to  $\frac{1}{2}$  drachm (1 to 2 g.).

The dried bark of *Z. americanum* or *Z. Clava-Herculis*. Carminative and gastro-intestinal stimulant producing diuresis and diaphoresis. A liquid extract has been used in the treatment of alcoholism.

## BENZENUM

B.P.C.

$C_6H_6 = 78.05$

*Syn.* BENZINE *Fr. Cx.* (Avoid this way of spelling, which is used in this country to denote the product obtained from petroleum—*vide infra.*)



**Dose.**—5 to 10 minims (0·3 to 0·6 ml.), in capsule or oily solution.

A colourless liquid obtained from light coal-tar oil. Sp. gr. 0·880 to 0·887. It solidifies at 0° and does not re-melt entirely below 4°.

Distinguish from **Petroleum Benzine** or **Benzoline**, the fraction of crude petroleum distilling below 150°. Light petroleum (petroleum ether) and petroleum benzine are used for heating cauteries for *navi*, etc. Benzene is not suitable for this purpose—it burns with a smoky flame. It is, however, better for removing grease stains.

**Antidotes.** Empty stomach by emetic, or by stomach tube, using a suspension of 10 oz. of medicinal charcoal in 2 gallons of water. Keep patient in fresh air, apply artificial respiration and give oxygen, or oxygen with 7% carbon dioxide, inhalations. Stimulants, *e.g.*,  $\frac{1}{2}$  dr. of aromatic spirit of ammonia in water. Atropine,  $\frac{1}{100}$  gr., hypodermically. Coramine intravenously is said to be of value—5 to 10 ml. of 25% solution.

When swallowed it usually produces a sensation of burning in the stomach. It is a narcotic which, when swallowed or inhaled, produces vertigo, delirium and tonic convulsions, followed by deep sleep; 30 ml. has proved fatal.

Benzene poisoning as an industrial hazard—*Lancet*, 11/1926, 558. Chronic benzene poisoning takes the form of aplastic anæmia when small quantities of benzene are inhaled over a prolonged period.—*Lancet*, 11/1927, 289.

**Uses.** For cough and whooping-cough, and in influenza. It quickly destroys pediculi capitis or pubis, applied freely; one application sufficient. For seborrhœa, should be brushed on the skin.

It has preservative action on organic matter.

Leukæmia has been treated by large doses, *e.g.*, 3 to 4 g. (45 to 60 minims approx.). Give small doses at first and note effects. As much as 2 dr. per day has been taken.

**Benzol** is a mixture of hydrocarbons obtained from light tar oil containing about 70% of benzene with toluene,  $C_6H_5CH_3$ , and other hydrocarbons. Various grades are obtainable, *e.g.*, 90% benzol, 50% benzol, etc., the figures indicating the proportion distilling below 100°.

**Cyclohexane.** *Syn.* HEXAMETHYLENE, HEXAHYDROBENZENE.  $C_6H_{12}$ . Is a colourless mobile liquid obtained by the hydrogenation of benzene. B.p. 81°. Is used as a solvent.

**Benzoyl Chloride.**  $C_6H_5COCl$  = 140·5. Prepared from phosphorus pentachloride and benzoic acid. Distils between 190° and 200°, sp. gr. 1·218. Distinguish from monochlorobenzene (*syn.* benzol chloride),  $C_6H_5Cl$  = 112·56, sp. gr. 1·106, b.p. 132°, and benzyl chloride,  $C_6H_5CH_2Cl$  = 126·5, sp. gr. 1·106, b.p. 178°; also benzal chloride (*syn.* benzylidene chloride or benzyl dichloride),  $C_6H_5CHCl_2$  = 161·0, sp. gr. 1·288, b.p. 206°.

**Paradichlorbenzenum (B.P.C.).**  $C_6H_4Cl_2$  = 146·9

Colourless shining crystals with characteristic odour, m.p. 53° to 54°, slowly volatile in air. **Soluble** in benzene, ether and hot alcohol.

**Wood-Beetle Insecticide.** Paradichlorbenzene 92%, soap 3%, paraffin wax 3%, cedar wood oil 2%. Used in Westminster Hall.

Paradichlorobenzene when vaporised is effective for killing lice in clothing.

Moles can be banished effectively by a teaspoonful placed in the runs at 6 to 8 feet intervals.

**Orthodichlorobenzene**, a heavy colourless liquid with characteristic odour, has also been used as wood and furniture preservative. A mixture of *o*-dichlorobenzene 9, soap 7, and oil of cedar wood 1 is effective against the death-watch beetle.

**Anocide**. A preparation containing the ortho compound for killing wood-beetles.

**Nitrobenzenum** (B.P.C.). *Syn.* NITROBENZOL, OIL OF MIRBANE  
 $C_6H_5O_2N = 123.0$ .

[P2] "Nitrobenzene."

[83] "Nitrobenzene—in substances containing less than 0.1% of nitrobenzene; soaps containing less than 1% of nitrobenzene"

Pale yellow liquid with an odour similar to benzaldehyde. Used as an insect repellent and as preservative in polishes, etc. Largely used in chemical manufacture. Poisoning may occur from absorption through the skin or by inhalation of the vapour. It is a dangerous poison if used in sweetmeats.

**Antidotes**. Empty stomach by emetic or stomach tube. Give stimulants, but no alcohol or oils. Artificial respiration and oxygen with 7% carbon dioxide inhalations, if necessary. Strychnine  $\frac{1}{4}$  gr. hypodermically. Blood transfusion.

**Toluenum** (B.P.C.). *Syn.* TOLUOL, METHYLBENZENE  
 $C_6H_5 \cdot CH_3 = 92.06$ .

A product of the distillation of coal tar, occurring as a colourless, mobile, highly inflammable liquid. B.p. about  $111^\circ$ , flash-point about  $7^\circ$ , sp. gr. about 0.87. Is used as a preservative of urine before chemical examination, and for sterilising catgut.

**Xylenum**. *Syn.* XYLOL, XYLOLUM (*P. Helv. V*). A mixture of *o*-, *m*-, and *p*-dimethylbenzenes,  $C_6H_4(CH_3)_2 = 106.1$ . B.p. about  $140^\circ$ . Has chemical and physical properties allied to benzene. The 1:2 xylene boils at  $141^\circ$ , 1:3 xylene boils at  $139^\circ$ , 1:4 xylene boils at  $138^\circ$ . Used as a microscopic cleaning agent and for sterilising catgut.

In dose of 5 to 15 minims in capsules, enteric-coated, has been employed in respiratory affections and in dyspepsia, and has also been suggested for use in certain skin diseases.

**Solvent Naphtha** consists of xylenes and trimethylbenzenes, b.p.  $140^\circ$  to  $180^\circ$ . Used as a solvent.

## BETANAPHTHOL

*B.P.*, *U.S.P. XI*, *Fr. Cx.*, *P. Belg.*, *P. Austr.*, *P. Helv. V*, *P. Dan.*,  
*P. Ned. V*, *F.E. VIII*, *P. Belg. IV*, *P. Ital. V*.

$C_{10}H_7OH = 144.1$ .

*Syn.* NAPHTHOL,  $\beta$ -HYDROXYNAPHTHALENE.

**Dose**.—5 to 10 grains (0.3 to 0.6 g.) in cachet. *Fr. Cx.* has max. single dose 15 grains, max. during 24 hours 45 grains approximately. *U.S.P. XI* average dose 4 grains.

**Manufacture.** Naphthalene is sulphonated at about  $180^{\circ}$  and the resulting  $\beta$ -naphthalene-sulphonic acid is fused at  $300^{\circ}$  with caustic soda

Occurs in white or nearly white crystalline lamellæ or powder with a faint phenolic odour.

**Soluble** about 1 in 1000 of water, 1 in 2 of alcohol 90%, 3 in 4 of ether, 1 in 17 of chloroform, 1 in 24 of benzene, 1 in 12 of olive oil and lard, 1 in 80 of soft paraffin; also soluble in glycerin and in solutions of alkali hydroxides. Addition of boric acid increases solubility in water.

**Incompatible** with camphor, ferric chloride, menthol, phenazone and phenol

**Uses.** Internally as intestinal antiseptic in enteric fever and putrefactive diarrhoea, safe and efficient, but sometimes causes too much gastric disturbance. In dilated stomach, dyspepsia and other disorders. In cholera, as preventive, and in treatment of early stages. Is a vermifuge in ankylostomiasis. Large doses may cause toxic effects with symptoms of phenol poisoning. In kidney disease it is contraindicated.

It is a powerful antiseptic and germicide. In advanced scabies, an ointment of 10 to 15% cures the eczema as well as destroys the parasite, but the Compound Ointment is preferred. Useful also in psoriasis and other chronic skin diseases.

Betanaphthol 5, alcohol 100, glycerin 10, is a remedy for hyperhidrosis of palms, soles and axillæ

Tablets of betanaphthol 5 grains (0.3 g) with phenolphthalein 3 grains (0.2 g)

To combat ankylostoma infection. A useful combination

**ANKYLOSTOMIASIS AND MALARIA.** 75% of malaria cases in Malay States are also ankylostomiasis cases. It may be that the ankylostoma worm is as much responsible for malaria as the mosquito. Quinine cannot be given in large or continuous doses. Best results with betanaphthol and Ol. Chenopodii.—D. Bridges, *Brit. med. J.*, ii/1921, 149.

**Betanaphthol treatment.** No untoward effect with 50 to 75 grain doses of the powdered drug. Ascaris infection treated with betanaphthol showed cure in a large percentage of cases.—C. N. Leach and G. E. Hampton, per *J. trop. Med. (Hyg.)*, 1923, 145. See also *ibid.*, 1922, 285.

**TRACHOMA** treated by "Oxidised Naphthol Camphor." The remedy should be freshly prepared, 2 parts of camphor and 1 of naphthol warmed gently and filtered, and the mixture allowed to oxidise in a clear glass vessel to syrup consistence and brown mahogany colour. The application is made with a small brush well soaked in the solution and then wiped nearly dry. Four to 10 applications suffice.—G. Gerard, *Prescriber*, 1920, 312.

**TÆNIA.** Betanaphthol, 15 grains for ten days, on an empty stomach, effectual after male fern had eliminated everything except the head.—J. W. Tomb, *Lancet*, i/1923, 1131.

**Tabellæ Betanaphtholis (B.P.C.).** Contain 5 gr. (0.3 g.)

**Unguentum Betanaphtholis Compositum (B.P.C.) Syn. KAPOSI'S COMPOUND OINTMENT, UNGUENTUM NAPHTHOL COMPOSITUM.**

Betanaphthol about 1 in  $11\frac{1}{2}$ , with chalk, in lard and soft soap. *L.H.* is practically identical.

**Unguentum Naphtholis (St. J.H.).** Betanaphthol 22 gr., sesame oil 6 dr., hard paraffin 30 gr., soft paraffin to 1 oz.

**Carbo Naphtholatus** (*P. Ital. V*). Betanaphthol 30, charcoal 40, magnesium oxide 30, mix, add alcohol 95% 50, and heat to form a coarse granular powder.

Given in doses of 1 to 2 dr in ailments of the stomach and intestines.

**Alphanaphthol** (*F E. VIII*). *Syn.*  $\alpha$ -HYDROXYNAPHTHALENE  
 $C_{10}H_7 \cdot OH = 144.0$ .

*Dose.*—2 to 5 grains (0.12 to 0.3 g.). Larger doses are sometimes given.

In colourless crystals, m.p. about 94°. Is said to have greater antiseptic power, but given internally causes more irritation.

This is also made from naphthalene on similar lines to  $\beta$ -naphthol. The sulphonation must be conducted at a *very low* temperature.

A solution of 1 in 3500 of water is used to wash out the intestines by rectal injection

**Aluminil Naphtholsulphonas.** *Prop Name* ALUMNOL (*Bayer Products, London*) A whitish powder soluble 1 in 1½ of water, and in alcohol or glycerin. A mild antiseptic in ¼ to 5% solutions. Used in solution or ointment, ¼ to 2%, in rhinitis, ozæna and gonorrhœa.

**Calcil Naphtholsulphonas.** *Dose.*—5 to 15 grains (0.3 to 1 g.)

White or reddish-white odourless neutral powder, soluble 1 in 1.5 of water and 1 in 3 of alcohol 90%.

**Betanaphthylis Benzoas** (*B.P.C., Fr. Cx., P. Ital. V, P. Belg. IV, P. Helv. V*). *Syn.* BENZONAPHTHOL, BENZOYL-NAPHTHOL, NAPHTHOL BENZOATE.  $C_{10}H_7 \cdot COOC_{10}H_7 = 248.1$ .

*Dose*—5 to 15 grains (0.3 to 1 g.) in cachet or suspended.

A tasteless white crystalline powder. Soluble in alcohol, ether, and chloroform, almost insoluble in water. An intestinal antiseptic and diuretic, *e.g.*, in typhoid. May be combined with bismuth salicylate. Externally is used 3 to 10% in ointments. Tablets, 5 grains, to be crushed and taken in a little water.

**Benzonaphthol Varnish.** Benzonaphthol 6, acetannin 10, salol 20, alcohol (90%) 30, ether 100, has been recommended as a varnish for pills to render them insoluble in the stomach, but no better results are obtained with it.

**Betanaphthylis Salicylas** (*B.P.C., Fr. Cx.*). *Syn.* BETOL, NAPHTHALOL, NAPHTHOL SALICYLATE.  $C_{10}H_7(OH) \cdot COOC_{10}H_7 = 264.1$ .

*Dose.*—5 to 10 grains (0.3 to 0.6 g.) in cachets or pills, or suspended in mixtures or in almond emulsion or milk.

In small tasteless white crystals.

**Insoluble** in water, slightly soluble in cold alcohol 90%, soluble 1 in 3 of boiling alcohol, 1 in 15 of ether, and in benzene. Useful in rheumatism, cystitis, and intestinal catarrh.

**Cachets of Betol and Bismuth Salicylate.** 5 grains each, useful as an intestinal disinfectant. Contraindicated in renal disease.

**Naphthalenum** (*B.P.C., P. Ned. V, P. Ital. V, P. Helv. V*).  
 $C_{10}H_8 = 128.1$ .

*Dose.*—3 to 12 grains (0.2 to 0.8 g.) in cachets.

A hydrocarbon formed in the manufacture of coal gas. In white crystalline plates (m.p. 80°) with persistent odour.

**Soluble** 1 in 3 of ether, 1 in 23 of alcohol, 1 in 8 of olive oil, and 1 in  $1\frac{1}{2}$  of chloroform; insoluble in water.

**Antidotes.** Empty stomach by emetic or stomach tube. Give purgative dose of magnesium sulphate. Demulcent drinks, but *not* oils or fats.

**Uses.** As an intestinal disinfectant for the diarrhoea of consumption and of typhoid, and for dysentery, 8-grain enemata are useful. Is painless in action, and promotes healing of ulcers. Internally, *e.g.* in malt extract, with success to lessen fœtor of urine and stools. A vermifuge in tænia and ascarides. Suppository and ointment (10%) are used for pruritus ani. A 10 to 20% solution in oil is successful as a parasiticide in scabies. The vapour is inhaled for whooping cough.

A precipitated form is also made by adding an alcoholic solution to water. For use as a dusting powder diluted 1 in 10.

**Naphthaleni Tetrachloridum (B.P.C.).** *Syn.* NAPHTHALIN HYDROCHLORIDE.  $C_{10}H_8Cl_4 = 269.9$ .

**Dose.**—3 to 12 grains (0.2 to 0.8 g.).

**Manufacture.** By chlorinating naphthalene 400 with potassium chlorate 800 and hydrochloric acid. *Data*, Edn. XIX, p. 573.

White crystals, m.p.  $185^{\circ}$  to  $187^{\circ}$ , insoluble in water.

Used for the same purposes as betanaphthol.

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## BISMUTHUM

Bi = 209.0.

### Metallic Bismuth Preparations for Injection.

Bismuth metal has been largely used in conjunction with, and in some quarters instead of, mercury in treatment of syphilis and yaws. The preparations used are summarised.

**Bismuthum Præcipitatum (B.P.).**

**Dose.**— $1\frac{1}{2}$  to 3 gr. (0.1 to 0.2 g.) by intramuscular injection.

Prepared by the reduction of bismuth trichloride in hydrochloric acid solution by means of hypophosphorous acid. A dull grey powder containing no particles greater than 15 microns in diameter.

Martindale obtained a preparation in which the average diameter of the particles was about 0.07 mm. by reducing a 1 in 10 solution of bismuth oxychloride in acidified water by warming it on a water-bath with four times the theoretical quantity of hypophosphorous acid added in small quantities at a time.

**Injectio Bismuthi (B.P.).** *Prop. Names.* BISGLUCOL (*Pharmaceutical Specialities (May & Baker) Ltd., London*), BISMOSTAB (*Boots, Nottingham*).

**Dose.**—8 to 15 m. (0.5 to 1 ml.).

Contains 20% w/v of precipitated bismuth with 0.5% v/v of cresol in isotonic dextrose solution.

**LOCAL NICKEL POISONING** (2 cases) due to use of nickel-plated piston for bismuth injections. An all-glass syringe should be used.—F. C. Eve, *Brit. med. J.*, ii/1929, 1030.

**Toxic Effects.** *Bismuth preparations, in general, are apt to cause gingivitis and stomatitis. Gingivitis is said to be less frequent with aqueous than with oily solutions. Care must be taken with the mouth.*

Severe stomatitis from injection of metallic bismuth may be treated by intravenous injections of 5 ml. of 10% sodium thio-sulphate solution on alternate days

The absorption rate of metallic bismuth is uniform, and action steady. In syphilitic affections of the heart and respiratory system bismuth is the only drug to fall back on. Only danger to avoid is injection into the blood stream, as it causes paralysis and death within two hours—C. F. Cheney, *Indian med. Gaz.*, 1926, 536

Soluble compounds are more toxic and painful than insoluble bismuth preparations. Metallic bismuth is the least toxic—should be given by deep subcutaneous route. Poisoning may occur in spite of absence of blue line. Tertiary lesions of mouth and tongue and symptoms of tabes respond particularly well. Valuable in nephritis, jaundice and organic disease where mercury and arsenic are not suitable. Not an efficient substitute for arsphenamine. May have an inhibitory rather than a curative effect. It is not established that bismuth is more effective than mercury in the permanent cure of syphilis—T. Anwyl-Davies, *Lancet*, i/1927, 200; *ibid*, 148.

Bismuth medication causes local pain; avoided by use of suitable preparations and careful technique. Toxic effects: a stomatitis may occur; colitis and nephritis have occasionally been reported, and also headache and depression.

Bismuth should not replace arsenic in all cases, being specially indicated in cases resistant to, or intolerant of, arsenic—Emory and Morin, *Paris méd.*, Dec., 1922, 509.

The urine should be watched during treatment—*Brit. med. J. Epit*, ii/1922, 58.

Bismuth compounds contraindicated in heart disease, being liable to induce weakness and irregularity of action—*Per Prescriber*, 1924, 57.

Peripheral polyneuritis following injection of metallic bismuth preparation. Risk of injections of bismuth preparations when kidneys are damaged—M. Critchley, *Brit. J. vener. Dis.*, Jan., 1926, 83.

Many cases of albuminuria recorded following bismuth administration.—*Brit. med. J. Epit*, i/1925, 77.

Injections of metallic bismuth are dangerous—probably true, though to less extent, of bismuth oleate. Bismuth salicylate is also dangerous, and should be replaced by a more soluble salt, e.g., potassium bismuth tartrate intragluteally once a week. Injection of insoluble bismuth salts twice weekly is open to question, as only a small amount is absorbed at most, and too frequent deposits may lead to cumulative action—*Per J. trop. Med. (Hyg)*, 1926, 161. See also G. A. Masson, *J. Pharmacol.*, Dec., 1926, 121.

Bismuth oxides must be used with caution. May produce abscesses. A bismuth course may consist of (a) a soluble compound in small repeated doses, (b) precipitated bismuth metal in aqueous suspension, for rapid results, (c) inorganic insoluble compounds, chiefly iodoquinates for prolonged and tonic treatment.—R. Barthelemy, *Urol. cutan. Rev.*, May, 1926, 310

### References to Uses.

**SYPHILIS.** Bismuth is more rapid in action on *S. pallidum in vivo* than mercury but not so rapid as Salvarsan. It influences lesions as rapidly as Salvarsan and more rapidly than mercury. It is free from danger in therapeutic doses—best given as metallic bismuth in isotonic glucose.—David Lees, *Brit. med. J.*, ii/1927, 298.

Superior to mercury in syphilis. Intramuscular the best route, preferably of compounds not quite insoluble in water—bismuth salicylate one of the best. Oxychloride specially good. Daily dose of bismuth metal fixed at 0.5 mg per kilo weight. Routine treatment a series of 5-6 intravenous injections of neocarsphenamine, in doses of 0.6 to 0.7 g. and a series of 8 to 10 intramuscular injections of bismuth oxychloride in watery suspension in dose of 0.15 to 0.2 g.,

with a total of 18 neoarsphenamine and 60 bismuth injections in 2 years. Definitely effective.—Svend Lornholt, *Brit. med. J.*, ii/1929, 890.

Syphilitic ocular conditions. Routine treatment, 12 weekly intramuscular injections of metallic bismuth and Sulfarsenol followed by a course of potassium iodide.—E. O. Kirwan, *Brit. med. J.*, ii/1931, 534.

Bismuth in the treatment of syphilis seems to have become the popular remedy, and in France positive harm seems to have been done by it, owing to the exclusion of the arsphenamines in early syphilis.—Leader, *Brit. med. J.*, ii/1932, 680.

YAWS. Cannot be cured by potassium iodide and mercury, but bismuth metal is effective. Three or more injections are needed and the treatment is used in Kenya and Tanganyika Territory on the lines of syphilitic treatment.—P. H. Manson-Bahr, *Brit. J. vener. Dis.*, Jan, 1928.

For details of a suggested course of combined treatment of syphilis with arsenic and mercury or bismuth, see under *Arsphenamina*, p. 215.

**Bicreol** (*Burroughs Wellcome, London*) Dose—1 to 2 millilitres intramuscularly, alternating with neoarsphenamine injections. Contains bismuth metal 0.15 g per ml in a Creol-Camph base.

**Bismoid** (*Lilly, London*). Bismuth metal in aqueous solution (1 ml = 0.025 g.).

**Neo-trépol** (*Chenal et Douhet, Paris; Anglo-French Drug Co., London*) is a 10% suspension of precipitated bismuth in isotonic solution. Given intramuscularly in doses of 1.5 to 2 ml. every 3 or 4 days.

The dose of Bi in different ampoules was inexact. Not admitted to N.R.—*J. Amer. med. Ass.*, i/1926, 136.

**Bi-Liposol** (*Modern Pharmaceuticals, London*) Oily solution of camphor-carbonate of bismuth (1 ml = 4 ctg Bi). Dose—2 ml intramuscularly twice a week. In syphilis and yaws.

**Biscam** (*Modern Pharmaceuticals, London*) A suspension of bismuth camphorate in olive oil. Dose—2 ml. intramuscularly every 3, 5, or 7 days for 12 to 18 injections. In syphilis and yaws.

**Bivatol** (*Laboratoire Français de Chimiothérapie, Paris; Anglo-French Drug Co., London*) Basic bismuth  $\alpha$ -carboxethyl- $\beta$ -methylnonoate. A lipo-soluble bismuth compound supplied in ampoules containing 2 ml. (= 0.07 g. of bismuth), for intramuscular injection in syphilis.

**Neo-cardyl** (*Pharmaceutical Specialities (May & Baker) Ltd., London*) Bismuth butylthiolaurate in oily solution (1 ml = 0.05 g. Bi). Dose—1.5 ml intramuscularly at 5-day intervals for 12 doses. Syphilis.

**Stabismol** (*Boots, Nottingham*) Basic bismuth  $\alpha$ -carbethoxy-cyclo-hexanyl acetate. 10% bismuth in olive oil. Dose—When given alone, from 1 to 2 ml weekly intramuscularly in doses of 0.5 to 1 ml. at intervals of 2 or 3 days, for from 4 to 8 weeks. Also given concurrently with the arsphenamines.

### Bismuth Salts and Compounds.

The absorbent action of the preparations of bismuth taken internally is increased by combination with antiseptic compounds. These combinations have been much recommended in those disorders of the digestive tract in which several infectious diseases make their early manifestation. Thus the salicylate, and naphthol, phenol, pyrogallol and bromophenol compounds have been brought into use. These check the fermentative processes forming ptomaines, yet, it is said, do not interfere with intestinal digestion.

Bismuth compounds are in general *incompatible* with potassium iodide, the insoluble brown bismuth tri-iodide being formed.

**BISMUTH POISONING.**—The most striking features are stomatitis, a black line and white diphtheritic membrane on the gums, and bismuth in the urine.

**Bismuthi Benzoas.** *Syn.* BISMUTH OXYBENZOATE.

$C_6H_5 \cdot COO(BiO) = 346.0$ .

*Dose.*—5 to 20 grains (0.3 to 1.2 g.) thrice daily.

A white powder insoluble in water, containing the equivalent of about 65% of  $Bi_2O_3$ . Antiseptic, internally in gastro-intestinal diseases, externally to chancroid, indolent and sloughing ulcers.

**Benzo-Bismuth** (*Anglo-French Drug Co, London*). Sodium salt of trioxymuthobenzoic acid. Ampoules contain 0.2 g (0.04 g. of Bi). *Dose*—1 ampoule intramuscularly twice weekly for 7 to 8 weeks, allowing a rest of 3 to 6 weeks between each series of 15 injections. In syphilis.

**Neo-Oleosal** (*Bayer Products, London*). 10% solution of bismuth dimethyl-endomethylene-hexahydrobenzoate in oil. *Dose*—2 ml. intramuscularly 2 or 3 times weekly up to a total dosage of 25 or 30 ml. In all stages of syphilis.

**Bismuthi Carbonas** (*B.P., U.S.P. XI, P. Helv. V, P. Dan., etc.*). *Syn.* BISMUTH OXYCARBONATE OR SUBCARBONATE. Composition varies slightly, but it approximates to  $(Bi_2O_2CO_3)_2, H_2O = 1038.1$ .

*Dose*—10 to 30 grains (0.6 to 2 g.)

The light varieties need no suspending agent.

*Uses.*—Internally in dyspepsia, gastric inflammation and diarrhoea, forming a protective coating on the walls of the stomach and intestines; also with alkalis in the treatment of gastric and duodenal ulcer. Externally, is sedative and astringent, in ointments and dusting powders. Has been used as a contrast medium in X-ray work.

**DYSENTERY** Bismuth subcarbonate is a most useful adjunct in acute dysenteric cases. Subnitrate of bismuth is not used because of possible untoward nitrite effects, such as methæmoglobinæmia and methæmoglobinuria, following the administration of excessive amounts of the drug in susceptible individuals.—H. A. Anderson, *J. trop. Med. (Hyg.)*, 1935, 271.

**ASCARIS AND STRONGYLIS.** Large doses, e.g., 30 g. in 24 hours, effective.—*Yearb. Pharm.*, 1926, 193.

**THREAD-WORMS** Bismuth carbonate, as suggested by Loeper, a specific. For an adult 3 doses of 20 gr. at intervals of 4 hours, and for a child under 7 years 10 to 40 gr. per dose. Simple and instantaneous cure.—G. Simpson, *Brit. med. J.*, ii/1929, 604. Correspondence on treatment.—*Brit. med. J.*, ii/1931, 517.

**X-RAY DIAGNOSIS** Bronchoscopic insufflation with bismuth carbonate of value in radiography of the lungs. One ounce can be safely used in adults.—*Brit. med. J. Epit.*, i/1926, 35.

**Enema Bismuthi** (*B.P.C.*) *Dose*—20 ounces (600 ml.)

Bismuth carbonate or subchloride 30% w/v in mucilage of starch.

**Glycerinum Bismuthi Carbonatis** (*B.P.C.*).

*Dose.*—10 to 60 minims (0.6 to 4 ml.)

Bismuth carbonate 50% w/v, in distilled water and glycerin.

**Mist. Bismuth.** (*N.I.F.*)

Bismuth carbonate 5 gr., sodium bicarbonate 10 gr., light magnesium carbonate 10 gr., peppermint water to  $\frac{1}{2}$  oz.

**Mistura Bismuthi cum Catechu** (*P.E.H.C.*) For 1 year old child.

Bismuth carbonate 5 gr., sodium bicarbonate 2 gr., tincture of catechu 3 m., compound tincture of cardamom 5 m., spirit of chloroform 1 m., glycerin 15 m., water to 1 dr.

[P1] **Mistura Bismuthi et Pancreatini** (*B.P.C.*).

*Dose.*— $\frac{1}{2}$  to 1 ounce (15 to 30 ml.).



Bismuth carbonate 10 gr., sodium bicarbonate 10 gr., pancreatin 4 gr., with dilute hydrocyanic acid, in chloroform water to 1 oz.

**Mistura Bismuthi et Sodii Bicarbonatis (B.P.C.).**

*Syn.* MISTURA BISMUTHI CUM SODA.

*Dose.*— $\frac{1}{2}$  to 1 ounce (15 to 30 ml.).

Contains 10 grains each of bismuth carbonate, sodium bicarbonate and light magnesium carbonate in 1 oz.

**Mist. Bismuth. Fort. (N.I.F.).**

Bismuth carbonate 10 gr., sodium bicarbonate 10 gr., heavy magnesium carbonate 10 gr., peppermint water to  $\frac{1}{2}$  oz

[P1] **Mist. Bismuth. Sed. (N.I.F.).**

Bismuth carbonate 5 gr., sodium bicarbonate 10 gr., chalk 5 gr., tincture of chloroform and morphine 10 m, water to  $\frac{1}{2}$  oz

[P1] **Mist. Bismuth. Sed. Fort. (N.I.F.)**

Bismuth carbonate 10 gr, sodium bicarbonate 10 gr, dilute hydrocyanic acid 2 m, solution of morphine hydrochloride 5 m, chloroform water to  $\frac{1}{2}$  oz

**Pasta Bismuthi (B.P.C.).**

Bismuth carbonate 30% in white soft paraffin

**Pulvis Bismuthi Compositus (B.P.C.).**

*Caution.*—This name was formerly applied to Ferrier's snuff.

*Dose.*— $\frac{1}{2}$  to 1 drachm (1 to 4 g).

Bismuth carbonate 1, calcium carbonate 3, heavy magnesium carbonate 3, sodium bicarbonate 1.

For the treatment of gastric and duodenal ulcer This is usually supplied for MacLean's powder *N.I.F.* has practically the same proportions, but specifies chalk instead of the purer calcium carbonate, thus agreeing with MacLean's original Formula II (for hospital use). Formula I contained bismuth carbonate 2, sodium bicarbonate 1, heavy magnesium carbonate 2 Administration of alkaline powders must be accompanied by dietary control, as in the following scheme (H. MacLean and co-workers, *Lancet*, 1/1928, 14; *Brit. med. J.*, i/1928, 619)

*First Week.* A teaspoonful in a little water or milk 6 or 7 times daily (preceded by a glass of milk with 10 grains sodium citrate added to prevent coagulation), with double dose last thing at night and extra powder during night if patient wakes. If bowels disturbed excessively, adjust powder or add magnesia cream *Second Week.* If discomfort and symptoms still persist continue as first week for a few days, otherwise reduce powder to 4 or 5 doses daily and reduce milk, adding beaten up eggs and gradually increasing diet so that by end of week patient is receiving toast, butter, eggs, custard, and cream. Dose immediately before retiring and during night as before. *Third Week.* Reduce to 3 or 4 doses daily and one at bedtime and increase food to include fish and potatoes and cereal puddings. *4th to 6th Weeks.* Powder 3 times daily, with dose at bedtime and reduce or give up milk. A small amount of meat may be taken the 5th week. *After-treatment.* Continue powder two or three times daily for further 6 weeks, with a dose at bedtime for a long time afterwards, and return to milk or light diet with powder 4 or 5 times daily if symptoms return at any

time. Smoking and alcohol should be avoided. Practically all uncomplicated ulcers can be cured in a comparatively short time by this treatment.

Criticism of the word "cure" and of omission of any reference to the "Sippy" Treatment (see page 622), which is on similar lines. Renal disease and pyloric stenosis contraindications—J A Ryle, *Lancet*, i/1928, 104, also T. Izod Bennett and A. Moncreff, *ibid*, 104. Reply to criticisms—no claim to originality; pyloric stenosis not found a contraindication. Main purpose to help the general practitioner—Hugh MacLean and co-workers, *ibid.*, 157.

The popular triple carbonate powder has many disadvantages. Sodium bicarbonate is the most powerful of all stimulants of gastric secretion and produces an enormous rise in acidity after the initial neutralisation, magnesium carbonate has the disadvantage of giving off carbon dioxide, and bismuth oxycarbonate is not an alkali at all, being completely inert as well as very expensive.—A. F. Hurst, *Practitioner*, ii/1933, 356

**Tabellæ Bismuthi Carbonatis (B.P.C.)** contain 5 gr. (0.3 g.).

**Tabellæ Bismuthi et Sodii Bicarbonatis (B.P.C.)** Dose—1 to 3 tablets.

Contain 2 gr. of bismuth carbonate and 3 gr. of sodium bicarbonate.

**Trochisci Alkalini Compositi (B.P.C.)**. Each lozenge contains 12 gr. of compound bismuth powder.

**Trochiscus Bismuthi Compositus (B.P.)**. Contains 2½ gr. each of bismuth carbonate and heavy magnesium carbonate and 4½ gr. of calcium carbonate

**Unguentum Bismuthi (B.P.C.)**

Bismuth carbonate 12½% in white soft paraffin

[P2] **Ung. Bismuth. c. Camph.** (N.I.F.) For hæmorrhoids

Liquefied phenol 18 m, camphor 3½ gr, bismuth carbonate ¼ oz, ointment of zinc oxide ½ oz, white soft paraffin to 1 oz.

[D P1 81] **Unguentum Bismuthi Morphinae et Cocainæ** (Allingham) Bismuth carbonate 20, morphine hydrochloride ½, cocaine hydrochloride 3, soft paraffin to 100. Useful as astringent in hæmorrhoids and for allaying irritation

**Antacid Lozenges** (Parke, Davis, London) Takadiastase, bismuth carbonate, magnesium carbonate, oleoresin of ginger and oil of peppermint Dose—1 to 3 lozenges To neutralise gastric acidity

**Cremo-Carbonates** (Sharp and Dohme, London) Each fluid ounce contains bismuth carbonate 20 gr, magnesium carbonate 20 gr calcium carbonate 10 gr, chloroform 1 m

**Sanusin Sempules** (British Drug Houses, London) Suppositories containing resorcinol, boric acid, balsam of peru, zinc and bismuth carbonate Useful in treatment of hæmorrhoids.

[P1] **Sedeff** (Martindale, London) contains morphine (½ gr. in 1 dr), bismuth and digestive ferments. Dose—1 to 2 drachms in water. A palatable granular effervescent preparation, for use in sickness and derangement of digestive functions.

**Tablets Bismuth, Pepsin and Cascara** (Martindale)

Dose—1 or 2 as required after meals

Bismuth carbonate 3 grains, pepsin 3 grains, cascara extract 1 grain. A useful digestive.

**Bismuthi Citras (B.P.C.)**

Dose.—2 to 5 grains (0.12 to 0.3 g.).

A white crystalline powder, yielding from 55 to 59% of  $Bi_2O_3$ . It is probably a monobismuthylcitric acid,  $H_2C(H_5O_7)(BiO)$ . Insoluble in water and alcohol 90%, but soluble in ammonia. It is astringent and stomachic

**Bismuth Citrate Gauze.**—May replace iodoform gauze, being non-toxic and without odour. May be left in uterine cavity at least five days and still be free from offensiveness. For use after curettings, in nasal and aural surgery and for burns. Strips are supplied 1, 2, 3 and 36 inches wide.

**Bismuthi et Ammonii Citras (B.P.C.)**

*Dose.*—2 to 5 grains (0.12 to 0.3 g.).

In soluble shining pearly or translucent scales containing 46 to 50% of  $\text{Bi}_2\text{O}_3$ .

**Elixir Bismuthi.** *Dose*—1 drachm (4 ml.)

Bismuth citrate 1, distilled water 8, solution of ammonia  $\frac{1}{2}$  or *q.s.* Dissolve, filter and add simple elixir *q.s.* to 30.

**Liquor Bismuthi Concentratus (B.P.C.)**

*Dose.*— $\frac{1}{4}$  to  $\frac{1}{2}$  drachm (1 to 2 ml.).

Is twice the strength of *Liquor Bismuthi et Ammonii Citratis*, containing the equivalent of 10 to 12% *w/v* of  $\text{Bi}_2\text{O}_3$ .

**Liquor Bismuthi et Ammonii Citratis (B.P.C.)**

*Syn.* LIQUOR BISMUTHI, LIQUOR BISMUTHI CITRATIS

*Dose.*— $\frac{1}{2}$  to 1 drachm (2 to 4 ml.).

Contains the equivalent of 5 to 6% *w/v* of  $\text{Bi}_2\text{O}_3$ . May be prepared by dissolving bismuth citrate 10% *w/v* in solution of ammonia and diluting to volume, filtering if necessary.

If prepared with the minimum amount of ammonia (as in *B.P.C.*) the solution will give a precipitate when dispensed with sodium bicarbonate; if slightly alkaline no precipitate is produced.

When prescribed with glycerin of phenol, the mixture quickly develops a blue coloration if exposed to light.—*Pharm. J.*, 11/1933, 73

**[P1] Mistura Bismuthi Composita (B.P.C.).**

*Dose*— $\frac{1}{2}$  to 1 drachm (2 to 4 ml.).

1 dr. contains  $\frac{1}{2}$  dr. of concentrated solution of bismuth,  $7\frac{1}{2}$  m. of tincture of nux vomica, and 2 m. of dilute hydrocyanic acid.

Is also available with pepsin 1 gr. per drachm (**Mistura Bismuthi Composita cum Pepsino B.P.C.**) and with 1 gr. of pepsin and  $\frac{1}{4}$  gr. of morphine hydrochloride per drachm (**Mistura Bismuthi Composita cum Pepsino et Morphina B.P.C.**)

These preparations are still ordered, but the action of the pepsin is seriously interfered with by the other ingredients.

**[P1] Mist. Pepsinæ Co. c. Bismutho (Hewlett, London)** is a similar preparation available with or without opium.

**[P1] Bisedia (Giles, Schacht, Bristol)** *Dose*—1 drachm (4 ml.) containing bismuth and pepsin with  $\frac{1}{4}$  gr. of morphine hydrochloride, 2 m. of hydrocyanic acid, and 5 m. of tincture of nux vomica.

**Bismuth and Pancreatin (Martindale).** *Dose*—1 to 2 drachms (4 to 8 ml.) Bismuth and ammonium citrate 4 gr., glycerin of pancreatin 15 m., cinnamon water 15 m., syrup 15 m., glycerin 15 m., and simple elixir to 1 dr.

An alkaline stimulant digestive combining the sedative properties of bismuth with the pancreatic ferment in a compatible form.

**Bismuthi et Cinchonidinæ Iodidum.** *Prop. Name* BISCINIOD (*Martindale, London*).  $\text{C}_{20}\text{H}_{24}\text{N}_2\text{O HI} + \text{BiI}_3 = 1011.9$ .

*Dose.*— $\frac{1}{2}$  to 1 grain (0.01 to 0.06 g.).

Yellowish-red powder insoluble in ordinary solvents, containing about 20% bismuth, 40% each iodine and cinchonidine.

**Bismuthi et Sodii Tartras (B.P.C.).**

**Caution.** This is the acid compound; to be distinguished from Bismuthi et Sodii Tartras (*B.P.Add.*) which is a neutral bismuthyltartrate. The acid compound is not suitable for injection.

**Syn.** SOLUBLE BISMUTH TARTRATE, ACID BISMUTH SODIUM TARTRATE.

**Dose.**—2 to 5 grains (0.12 to 0.3 g.) *per os*.

The alkali bismuth tartrates may be divided according to method of making and use (*cf.* Corfield and Adams, *Pharm. J.*, 11/1923, 82).

(1) "NEUTRAL" compounds, termed "bismuthyl tartrates," or "tartrobismuthates," which are either soluble or insoluble in water, for injection in protozoal diseases. They are made by dissolving bismuth oxytartrate in alkali, the alkali bismuthyl tartrate resulting by evaporation or by precipitation with alcohol.

(2) "ACID" preparations, described as "bismuth tartrate soluble," in scales giving an acid solution. These are used with pepsin for digestive complaints. Bismuth tartrate, obtained by interaction of bismuth subnitrate and tartaric acid, is dissolved in sodium hydroxide solution and treated with excess of tartaric acid, the resulting solution being evaporated.

Colourless scales with acid reaction containing 38 to 44% of Bi.

**Soluble** in water.

**Uses.** For digestive complaints, in conjunction with pepsin, the acid solution favouring the action of the enzyme with which it is compatible in moderate amount.

**Liquor Bismuthi Acidus (B.P.C.)**

**Dose.**— $\frac{1}{4}$  to  $\frac{1}{2}$  drachm (1 to 2 ml.).

A solution of acid bismuth sodium tartrate, containing the equivalent of 9 to 10% *w/v* of  $\text{Bi}_2\text{O}_3$ .

**[P1] Mistura Bismuthi Composita Acida cum Pepsino (B.P.C.).**

**Dose.**— $\frac{1}{2}$  to 1 drachm (2 to 4 ml.).

One drachm contains acid solution of bismuth equivalent to about 5 gr. of bismuth sodium tartrate, 1 gr. of pepsin, and  $\frac{1}{2}$  m. of liquid extract of *nux vomica*.

The acidity of the mixture maintains the activity of the pepsin.

**Bismuthi et Sodii Tartras (B.P.Add.)**

**Caution.** This is the neutral compound; to be distinguished from Bismuthi et Sodii Tartras (*B.P.C.*) which is an acid bismuthyltartrate.

**Syn. and Prop. Name** BISMUTH SODIUM TARTRATE, SODIUM BISMUTHYL TARTRATE, SODIUM TARTROBISMUTHATE, SOBITA (*Howards, Ilford*).

**Dose.**—1 to 3 grains (0.06 to 0.2 g.) by intramuscular injection.

A white powder or yellowish scales containing 35 to 42% of Bi.

**Soluble** 1 in less than 1 of water.

**Uses.** Is administered intramuscularly in the treatment of syphilis. May be dissolved in water, saline or dextrose solutions, or

suspended in oil. Only suspensions are commonly preferred because less painful, and more slowly absorbed, hence less likely to cause toxic symptoms. Employed as a 1.5% solution, or stronger in suspension. The injections exert a marked diuretic action.

**DIURESIS.**—In doses of 0.03 g. intramuscularly bismuth sodium tartrate has a powerful diuretic action, more effective than Novasurol and with no ill effects except occasionally a local abscess at site of injection.—Clifford Hoyle, *Practitioner*, 11/1933, 428. See also P. J. Hanzlik and co-workers, *J. Amer. med. Ass.*, 1/1929, 1416.

**SYPHILIS, AORTIC.**—Pain, the most common symptom in 100 cases of aortic syphilis, was relieved in all but one case by sodium bismuth tartrate intramuscularly in doses of 2 ml. of a 1.5% solution twice a week in courses of 10 injections.—L. M. Blackford and J. H. Boland, *J. Amer. med. Ass.*, 11/1932, 1902.

**WARTS.**—The skin just outside the zone of hyperkeratosis is pierced with a fine hypodermic needle directed downwards and inwards towards the base of the warts and from  $\frac{1}{4}$  to 2 minims of a 1.5% solution of bismuth sodium tartrate is injected. A dark hemorrhagic area is seen in from 1 to 3 days after the first injection and after 7 to 14 days' treatment the wart either drops off or may be removed.—H. Shellow, per *Prescriber*, 1935, 332.

**Bismuthi et Potassii Tartras (U.S.P.XI)** *Syn.* POTASSIUM BISMUTH TARTRATE, POTASSIUM BISMUTHYL TARTRATE

*Average dose.*— $2\frac{1}{2}$  grains (0.15 g.) by injection.

A white powder *soluble* 1 in 2 of water. Contains the equivalent of 71 to 75% of  $\text{Bi}_2\text{O}_3$  (about 64 to 67% of  $\text{Bi}$ ). Given intramuscularly in syphilis in solution or suspension, as the sodium compound. It is stated to disappear completely from the site of injection, usually in 2 weeks.

**Sodium Potassium Bismuthyltartrate.** *Syn.* SODIUM POTASSIUM TARTROBISMUTHATE.

*Dose.*— $1\frac{1}{2}$  to 3 grains (0.1 to 0.2 g.) intramuscularly, in solution in saline, or in suspension in 1 to 2 ml. of vegetable oil. Is injected once or twice weekly until 30 to 45 gr. has been given.

A white powder *soluble* about 1 in 2 parts of water, giving a neutral solution.

Used in syphilis, but the difference in effect between it and a body without the potassium compound is no doubt negligible.

**EPILEPTIC MANIACS** and allied sufferers in the Tanganyika Territory were found to benefit from sodium potassium bismuth tartrate.—J. G. McNaughton, June 16, 1929.

**RELAPSING FEVER.** Sodium potassium bismuth tartrate brings fever down. Given intramuscularly—for an adult, 2 injections of 0.2 g. in 2 ml. water, for a child of 2 to 10 years 2 injections each of 0.1 g. For a baby under 2 years, 1 injection of 0.1 g.—J. Todd, *Brit. med. J.*, 1/1930, 312.

**YAWS** in Kenya Colony well treated.—R. Howard, *Trans. R. Soc. trop. Med.*, Mar., 1923, 437; C. R. Steel, *J. trop. Med. (Hyg.)*, 1927, 274.

**Bismutol Sterules** (*Martindale, London*). Ampoules containing 3 grains (0.2 g.) of sodium potassium bismuthyl tartrate in 2 ml. of sterile oil.

**Trépol** (*Chenal et Doullhet, Paris; Anglo-French Drug Co., London*). Only suspension of bismuth oxytartrate for intramuscular injection in syphilis and yaws.

Trépol is essentially basic bismuth carbonate and not as stated.—*J. Amer. med. Ass.*, 1/1926, 136.

**PSORIASIS** successfully treated by intramuscular injections. Complete retrogression of lesions in 12 and partial retrogression in 9 out of 21 cases. No local treatment.—*Lancet*, 11/1926, 559.

[P1 81] **Bismuthi Arsanilas.**  $\text{BiO} \cdot \text{O} \cdot \text{AsO}(\text{OH}) \cdot \text{C}_6\text{H}_4 \cdot \text{NH}_2 = 441 \cdot 0$ .

A white powder containing the equivalent of 53% of  $\text{Bi}_2\text{O}_3$  and 17% of As.

Prepared by interaction between bismuth sodium tartrate and sodium aminarsonate. It is best given as a suspension of the freshly precipitated compound containing 1 grain (0.06 g.) in 15 minims (1 ml.).

**Dose.**—Intramuscularly for adults 2 to 3 ml., for grown-up children 1 ml., for young infants 0.5 ml.

For use in syphilis and yaws

An injection consisting of 3 grains bismuth sodium tartrate and 2 grains Soamin, in 1 ml. water, given every 2nd day, almost invariably cleared up yaws in 6 days, and 75% of 538 cases of tertiary or congenital syphilis were completely healed in 12 days —J. O. Shircore, *Lancet*, 11/1926, 43.

300,000 cases of yaws treated with bismuth since 1922. The Soamin and bismuth sodium tartrate preparation costs less than a penny per dose —J. O. Shircore, *Lancet*, 11/1926, 43.

**Quinine Iodobismuthate** (*Fr. Cx. Supp.* 1926, *P. Belg. IV, F.E. VIII*).  $(\text{BiI}_3)_2 \cdot \text{C}_{20}\text{H}_{24}\text{N}_2\text{O}_2 \cdot 2\text{HI} = 1759 \cdot 7$ .

A bright red powder insoluble in water. Decomposed slowly on prolonged contact with water. Contains about 23% of Bi, 57% of I and 18% of quinine.

Method of preparation is given in *Fr. Cx. Supp.*

For intramuscular injection as a suspension in sterile oil in syphilis. Contraindicated in pulmonary tuberculosis and the following when not due to syphilis: advanced diseases of the heart and nervous system, nephritis, severe diabetes, cachexia.

**SUSPENSION D'IODOBISMUTHATE DE QUININE** (*Fr. Cx. Supp.* 1926).

Sterilise the pestle and mortar by burning a little spirit in the latter, and incorporate quinine iodobismuthate 17 g. with anhydrous wool fat 5 g., and neutral olive oil 87 g., making up to 100 ml. 1 ml. contains approx. 0.04 g. of Bi.

Iodo-bismuthate of quinine gave good results in some cases apparently drug-fast to arsenic and mercury —Col. E. T. Burke, *Lancet*, 1/1924, 902.

Good results confirmed —Margaret Rorke, *ibid*.

**Bismosalvan** (*Richter, London*), **Quinostab** (*Boots, Nottingham*), **Spirobismol** (*Homburg Pharma, London*) and **Rubyl** (*Pharmaceutical Specialities (May & Baker) Ltd, London*) are 10% suspensions of quinine iodobismuthate in olive oil. **Average dose** —3 ml. by intramuscular injection once or twice weekly for a course of 15 to 24 injections. **Steriles of Quinine Iodobismuthate** (*Martindale, London*) contain 0.17 g. in 1 ml.

**Neobismosalvan** (*Richter, London*) and **Spirobismol S.S.** (*Homburg Pharma, London*) are similar preparations containing also lecithin.

**Sodium Iodobismuthite.** *Syn.* SODIUM BISMUTH IODIDE.

A red crystalline compound consisting chiefly of hydrated  $\text{Na}_2\text{BiI}_6$ . Prepared by the interaction of bismuth iodide or chloride with dry sodium iodide in anhydrous ethyl acetate solution. Contains about 21% of Bi. **Soluble** 1 in 1 of water, giving a black precipitate of bismuth iodide on diluting and a red precipitate of oxyiodide on further diluting. For use in syphilis.

Preparation of sodium iodobismuthite —P. J. Hanzlik *et al.*, *J. Amer. med. Ass.*, 1/1932, 537.

**Iodobismitol with Saligenin** (*Squibb, New York, Martindale, London*) 2 ml. ampoules containing a solution of sodium iodobismuthite 0.12 g., sodium iodide

0.24 g., saligenin 0.08 g. (as local anæsthetic), in propylene glycol. *Suggested dose*.—2 ml. intramuscularly two or three times weekly for 12 injections.

Found as efficacious as any bismuth compound hitherto tried —G C Johnson *et al.*, *J. Pharmacol.*, 1932, 45, 469.

**Bismuthi Hydroxidum (B.P.C.).** *Syn.* BISMUTHUM HYDROXYDATUM, HYDRATED BISMUTH OXIDE.

*Dose*.—5 to 20 grains (0.3 to 1.2 g.).

A yellow (partly hydrated) or white (hydrated) bismuth oxide usually containing a large proportion of carbonate.

**Insoluble** in water. Soluble in acids and in alkalis in presence of glycerin.

**Uses**.—A substitute for bismuth carbonate; also injected intramuscularly in syphilis.

LUPUS ERYTHEMATOSUS treated by 12 bismuth hydroxide injections of 3.75 grains, 2 injections a week cured. Better than arsenic —*Brit. med. J. Epit.*, ii/1927, 29.

SYPHILIS. Suspended in water and glycerin stated to be preferable to the oily preparations —Svend Lomholt.

**Mistura Bismuthi Hydroxidi (B.P.C.).** *Syn.* MAGMA BISMUTHI.

*Dose*.—1 to 2 drachms (4 to 8 ml.).

A suspension of freshly precipitated hydrated oxide, free from carbonate, containing the equivalent of 10% w/v of  $\text{Bi}_2\text{O}_3$ .

Does not liberate carbon dioxide in the stomach.

**Mistura Bismuthi et Magnesii Hydroxidum (B.P.C.).**

*Dose*.—1 to 2 drachms (4 to 8 ml.).

Equal parts of mixture of bismuth hydroxide and mixture of magnesium hydroxide.

The magnesium hydroxide counteracts the constipating effect of the bismuth hydroxide.

**Bismosal (Arnfield & Sons, Stockport)** *Dose*.— $\frac{1}{2}$  to 1 drachm (2 to 4 ml.) Children 5 to 20 minims (0.3 to 1.2 ml.). Contains bismuth as hydroxide in suspension with salol. In diarrhoea.

**Bismosan (Roberts, London)** Ampoules containing bismuth hydroxide 3 gr. in 2 ml.

**Casbis New (Bayer Products, London)** Oily suspension of bismuth hydroxide (10% Bi). *Dose*.—0.5 to 1 ml. by intragluteal injection.

**Muthanol (Bengué, London)** Suspension of bismuth hydroxide and mesothorium bromide in olive oil for intramuscular injection in syphilis.

**Soderseine (Pecoul, Paris, Wilcox, Jozeau, London)** Colloidal suspension of bismuth sesquioxide. *Dose*.— $\frac{1}{2}$  to 2 oz. Treatment of whooping cough.

**Bismuthi Naphtholas (B.P.C.).** *Syn. and Prop. Name* NAPHTHOL-BISMUTH, BASIC BISMUTH BETANAPHTHOLATE, ORPHOL (*Heyden, Dresden; Braun, London*)

$\text{Bi}_2\text{O}_3(\text{OH})\text{C}_{10}\text{H}_7\text{O} = 610.1$

*Dose*.—5 to 15 grains (0.3 to 1 g.) in a cachet.

A pinkish-brown almost tasteless odourless powder, insoluble in water, slightly soluble in alcohol 90%.

A useful antiseptic and astringent for the stomach and intestines.

**Bismuthi Nitras Crystallisatus (Fr. Cx., P.G. VI)** *Syn.* BISMUTHI NITRAS NEUTRUS (*F.E. VIII, P. Ital. V*).

$\text{Bi}(\text{NO}_3)_3 \cdot 5\text{H}_2\text{O} = 485.1.$

*Dose* —5 to 10 grains (0.3 to 0.6 g.).

In colourless deliquescent crystals, which, if dissolved in a small quantity of water, give a solution with an acid reaction; this on further dilution throws out basic bismuth subnitrate. It is practically insoluble in alcohol 90%, but soluble in cold glycerin. *cf.* Glycerinum Bismuthi Nitratis *infra*. It is astringent and antiseptic, and useful for the diarrhoea of phthisis.

**Glycerinum Bismuthi Nitratis.**

Bismuth nitrate in crystals 1, glycerin to 4. Diluted 4 or 5 times with glycerin is a stimulant application in eczema and for chapped hands.

**Bismuthi Oxidum** (*B.P.C.*)  $\text{Bi}_2\text{O}_3 = 466.0$

*Dose* —5 to 20 grains (0.3 to 1.2 g.).

Is prepared by boiling bismuth subnitrate in solution of sodium hydroxide, washing and drying the deposited yellowish bismuth oxide. May be precipitated with acid from an alkaline solution containing glycerin.

**Anderson's Ointment.**

Bismuth oxide 1, oleic acid 8, white wax 3, white soft paraffin 9. In pruritus.

**Bismuthi Oxyiodogallas** (*B.P.C.*, *P. Jap. IV*, *P. Helv. V*, *P. Ned. V*, *P.G. VI*)  $\text{C}_6\text{H}_2(\text{OH})_3\text{COOBi} \cdot \text{OH} \cdot \text{I} = 521.7.$

*Syn. and Prop. Name* BISMUTH OXYIODOSUBGALLATE, AIROL (*Hoffmann-La Roche, London*), AIROFORM, AIROGEN.

A light greyish-green powder, odourless, tasteless, and non-irritant. It darkens on exposure to air. **Insoluble** in water, alcohol and ether. Used as ointment for ulcers, boils, whitlows, chancres, and intertrigo. Also as dusting powder, *e.g.*, for gonorrhoeal ophthalmia.

**Suppositoria Hæmorrhoidalia** (*Martindale*).

Bismuth oxyiodogallate 6, resorcinol 1.5, zinc oxide 6, balsam of Peru 1.5, yellow beeswax 0.0075, sesame oil 1.5, oil of theobroma 19 g. Divide into twelve suppositories.

**Anusol Suppositories** (*Warner, London*)

For hæmorrhoids. For composition, see Vol II.

**Noviform** (*Heyden, Dresden, Braun, London*) Bismuth tetrabrompyrocatechin (contains equivalent of about 30% of  $\text{Bi}_2\text{O}_3$ ). Antiseptic dusting powder and as 5% ointment for ophthalmic use.

**Bismuthi Phenas.** *Syn.* PHENOL-BISMUTH.

*Dose* —5 to 20 grains (0.3 to 1.2 g.).

A white powder, insoluble, containing a variable amount of phenol, combined with bismuth oxide. Acts slowly on the digestive tract and does not cause carboluria.

The exact formula of the compound is uncertain. Products with the highest phenol content are obtained by precipitation from neutral solution in the cold. The figures do not agree with  $\text{Bi}(\text{OH})_2\text{C}_6\text{H}_3\text{O} \cdot \text{C}_6\text{H}_5$ . E. Corfield and G. R. Boyes, *Pharm. J.*, 1/1921, 483.

**Bismuthi Sulphocarbolas.** *Syn.* BISMUTH PHENOLSULPHONATE

*Dose* —4 to 8 grains (0.25 to 0.5 g.) in cachets.

A red-tinted slightly soluble powder used in intestinal affections.

**Bismuthi Salicylas** (*B.P.*, *U.S.P. XI*, *P. Helv. V*, *P.G. VI*, *P. Ital. V*, *P. Dan.*, *P. Belg. IV*, *P. Ned. V*, *P. Jap.*).

*Syn.* BISMUTH OXYSALICYLATE, or SUBSALICYLATE. The formula approximates to  $\text{C}_6\text{H}_4 \cdot \text{OH} \cdot \text{COO} \cdot \text{BiO} = 362.0.$



**Dose.**—10 to 30 grains (0.6 to 2 g.) orally, 1 to 2 grains (0.06 to 0.12 g.) by intramuscular injection

A white powder, insoluble in water, alcohol, and glycerin, yielding on incineration about 64% of  $\text{Bi}_2\text{O}_3$ . Useful internally *per os* in some forms of diarrhoea, typhoid fever and gastric catarrh, and as a substitute for iodoform. A good intestinal antiseptic. Is given intramuscularly in syphilis in oily suspension.

**Suppositories of Bismuth Salicylate.** 10 grains in each  
A useful astringent in dysentery.

**Injectio Bismuthi Salicylatis (B.P.)**

**Dose.**—10 to 20 minims (0.6 to 1.2 ml) by intramuscular injection.

Contains 10% *w/v* of bismuth salicylate suspended in a sterile solution of camphor 1%, and phenol 1%, in olive oil.

**LICHEN PLANUS** Usually cured by a course of 10 to 12 weekly intramuscular injections of  $1\frac{1}{2}$  grains bismuth salicylate in olive oil—H. D. Grossman, *per J. Amer. med. Ass.*, 11/1932, 1203

**Pilula Bismuthi-Sodii Salicylatis cum Salol (Martindale)**

**Syn.** COMPOUND BISMUTH PILL.

**Dose.**—Two immediately after each of 6 consecutive meals, then discontinued for 2 days and repeat in the same manner

This pill contains in the centre bismuth carbonate  $2\frac{1}{2}$  gr., coated thinly with gelatin, and around this is a layer of sodium salicylate 2 gr., covered finally with salol  $1\frac{1}{2}$ ,  $2\frac{1}{2}$  or 3 gr., or as desired (*the salol to be applied pure by means of heat only*).

It was devised to ensure its reaching the part of the intestine affected by the catarrh. It is coated with acid-resisting material and it dissociates on meeting the alkaline intestinal juice. The well-known coating effect of the bismuth carbonate on the inflamed mucous surfaces is enhanced by the sodium salicylate. The bismuth remains *in situ* for from 8 to 10 days.

**Bisantal (Pharmaceutical Specialities (May & Baker) Ltd, London)**

Suspension of bismuth salicylate in oil for intramuscular injection containing 0.057 g of Bi per ml

**Bismogenol (Tosse, Hamburg, Pharmaceutical Products, London)** Suspension of bismuth salicylate in olive oil, stated to contain 6% of Bi

**Bisuspen (Heyden, Dresden, Braun, London)** Suspension of bismuth salicylate in oil 1 ml = 0.06 g of Bi. **Dose.**—8 to 12 injections of 0.5 to 1 ml intramuscularly at 3 to 4-day intervals

**Gastrozan (Heyden, Dresden, Braun, London)** Bismuth bisalicylate. Contains about 48% of bismuth oxide and 50% of salicylic acid. **Dose.**—0.5 to 0.75 g. Daily dose up to 3 g. Gastro-intestinal antiseptic

**Measurol (Bayer Products, London)** Basic bismuth methoxyhydroxybenzoate. Administered intramuscularly as a 20% emulsion in the treatment of syphilis.

**Bismuthum Subsaliylicum, Basic (Fr. Cx)**

$\text{C}_6\text{H}_4\text{OHCOO Bi(OH)}_2 = 380.1$

**Dose.**—5 to 20 grains (0.3 to 1.2 g.)

An amorphous anhydrous insoluble white powder neutral to litmus, incompatible with acids.

**Bismuthi et Cerii Salicylas.**

**Dose.**—5 to 20 grains (0.3 to 1.2 g.)

For sickness, diarrhoea, dysentery, and ulceration of the bowels

**Bismuthi Oxychloridum (B.P. Add.)**

**Syn.** BISMUTH SUBCHLORIDE (B.P.C.)  $\text{BiOCl} = 260.4$ .

**Dose.**—10 to 30 grains (0.6 to 2 g.), by intramuscular injection,  $1\frac{1}{2}$  to 3 grains (0.1 to 0.2 g.).

An amorphous or minutely crystalline powder insoluble in water, soluble in dilute acids. Pearl white or "*blanc de perle*" is bismuth subchloride precipitated by adding hydrochloric acid to a solution of the nitrate; "*blanc d'Espagne*" or flake white is precipitated with sodium chloride.

Given internally it produces a coating on the irritated parts of the stomach or bowels. As insufflation to the larynx  $\frac{1}{4}$  to 1 gr.

**LUPUS ERYTHEMATOSUS** The best tolerated salt of bismuth is the oxychloride suspended in water, with chlorbutol added to relieve pain on injection. The patient should be kept under a heavy bismuth dosage for 10 or 12 weeks, injections equivalent to 0.2 or 0.3 g. of bismuth being given once or twice weekly to a total of 3 or 4 g. in a series of 10 or 12 injections. After an interval of 6 weeks another course may be given.—R. M. B. MacKenna, *Med. Pr.*, 1935, 248.

Bismuth is the metal of choice. It is less toxic than gold, does not light up an existing tuberculous focus, and there is not the same risk of focal reaction.—A. G. Smith, *Brit. J. Dermat.*, 1934, 399.

**SYPHILIS** Bismuth oxychloride preferred in syphilitic treatment. It is probably reduced to metal. Course of 4 g. in 10 injections. Give concurrently with arsphenamine, rather than bismuth or mercury to follow. Quinine iodo-bismuthate has disadvantage of low bismuth content.—L. W. Harrison, *Lancet*, 1/1930, 764.

### **Injectio Bismuthi Oxychloridi (B.P. Add.)**

**Dose.**—15 to 30 minims (1 to 2 ml.), by intramuscular injection.

Bismuth oxychloride 10%, w/v with dextrose and cresol in sterilised water.

### **Mucilago Bismuthi.**

For X-ray diagnosis.

Bismuth oxychloride  $1\frac{1}{2}$  to 2 or 3 ounces or more made into a thick paste with acacia mucilage for a dose, for determining condition of the oesophagus and for examining shape, position and motor function of the stomach. A special bismuth oxychloride *free from nitrate* is made for X-ray work. It is inert in the stomach.

Bismuth in bread and milk in proportion of  $1\frac{1}{2}$  oz. of bismuth oxychloride to  $\frac{1}{2}$  pint of bread and milk to form a thick paste—not a liquid—is also employed and is in some respects more suitable.

In tuberculous joints bismuth injections are useful for diagnosis and treatment.

See also Bismuthi Carbonas *antea*, and *Radiology*, Vol. II.

### **Unguentum Bismuthi Oxychloridi.**

Bismuth oxychloride 1, white soft paraffin 15.

Is useful for anointing the speculum for vaginal examinations.

**B.C.C. Dusting Powder** (*Blythswood Chemical Co., Glasgow*) contains bismuth oxychloride, talc, light magnesium carbonate and boric acid. For nursery and general use.

**Bismurung** (*Blythswood Chemical Co., Glasgow*). An ointment of bismuth oxychloride 10% in colloidal dispersion, for chronic lupus erythematosus, rubbed in for at least 2 minutes twice daily. Also for general use as a sedative and antiseptic ointment. **Bismurung-Tropical** is the same as Bismurung, but has the melting point of the base adjusted to make it suitable for tropical climates. It is of value in "prickly heat."

Pustular folliculitis cleared up; tinea unguium and chancroids also treated. May be of value in yaws.—R. M. B. MacKenna, *Lancet*, 1/1931, 126.

**Bisoxyl** (*British Drug Houses, London*). A suspension of bismuth oxychloride in chlorbutol solution containing 0.1 g. per ml. Initial dose 0.1 g., increased to 0.2 g., corresponding to 0.01 and 0.02 g. of the bismuth salt. For syphilis and yaws.

**Chlorostab** (*Boots, Nottingham*). Bismuth oxychloride suspension in isotonic glucose solution in two strengths 1 ml. = 0.16 g of Bi metal and 1 ml. = 0.2 g. *Dose*.—1 injection (= 0.40 g of Bi) intramuscularly per week for 10 weeks; or 2 injections (each = 0.20 g. of Bi) per week for 10 weeks. *Dose* for children according to age and body weight, *e.g.*, from 1 to 4 years the equivalent of 0.05 g of Bi metal; from 4 to 8 = 0.06 to 0.07 g. Bi metal, over 8 years = 0.10 to 0.20 g. In syphilis, congenital syphilis, etc.

**Nascent Bismuth Oxychloride.**

Pain and vomiting due to catarrh or organic disease of the stomach treated by bismuth oxychloride in fine suspension made in nascent state by using Liquor Bismuthi and dilute nitrohydrochloric acid *q.s.* The mixture suggested is Liq. Bismuthi 6 dr., dilute nitrohydrochloric acid  $1\frac{1}{2}$  dr. or *q.s.*, peppermint water to 6 oz. One half ounce in water *t.d.* shortly before or after meals. (In dispensing, the acid is to be diluted and added last so as to throw out the bismuth as a dense white cloud).—H. O. Nicholson, *Prescriber*, June, 1920

**Bismuthi Subgallas** (*B.P.C., U.S.P. XI, P. Helv. V, P. Ital. V, P. Ned. V, P. Dan., Fr. Cx., F.E. VIII, P.G. VI, P. Belg. IV, P. Jap.*).  $C_6H_5(OH)_3COO \cdot (BiO)_3H_2O$  or  $Bi(OH)_3 \cdot C_6H_5O_3 = 412.1$ . *Syn. and Prop. Name* BISMUTH OXYGALLATE, DERMATOL (*Bayer Products, London*)

*Dose*—10 to 30 grains (0.6 to 2 g.)

**Manufacture.**—Bismuth carbonate 258 and gallic acid 188 are heated in presence of water 2000, until interaction has occurred.

The *Fr. Cx.* method is also satisfactory. Dissolve bismuth nitrate *cryst.* 100 g. in glacial acetic acid 200 g. Dilute with water 500 ml. and add with stirring gallic acid 37 dissolved in water 1500 ml. Wash the ppt. until the liquor is no longer acid to litmus. Dry at not exceeding 60°. *P. Ital.* method is similar.

An odourless, yellow, insoluble, non-irritant antiseptic dusting powder, employed alone or with starch.

**Incompatible** with alkaline sulphur compounds

Given internally for diarrhoea in doses of 30 to 90 grains daily. Emulsion of bismuth subgallate 2, acacia 2, water 25, has been used in gonorrhoea, with good results.

In ulcerative colitis an emulsion may be used to adhere to the mucosa; also of value after pile operations. Promotes healing.

**YAWS.** Dermatol intramuscularly gave as good results as the arsenicals.—*Per J. trop. Med. (Hyg.)*, 1925, 35

Collapsible tubes, with catheter attachment, of bismuth subgallate ointment (10%), with paraffin basis, are useful in gonorrhoea, this ointment is also good for burns and eczema

**Carbasus Bismuthi Subgallatis.** BISMUTH SUBGALLATE GAUZE

To prepare, use an emulsion of bismuth subgallate,  $\frac{1}{2}$  to 1 of glycerin to 2 of alcohol (90%) and proceed in the customary manner—the final strength being 10 to 20% of bismuth in the gauze as required. For packing cavities

**Suppositorium Bismuthi Subgallatis** (*B.P.C.*) 5 grains

**Suppositorium Bismuthi Subgallatis Compositum**

(*B.P.C.*). *Syn.* SUPPOSITORIUM BISMUTHI ET RESORCINI COMPOSITUM.

Bismuth subgallate 3 gr., resorcinol 1 gr., zinc oxide 2 gr., and balsam of Peru 1 m. in each suppository.

[P1] **B.F.I.** (*Sharp & Dohme, London*) Bismuth-formic-iodide compound Bismuth-formic-iodide 70 gr., acetanilide 30 gr., zinc sulphocarbolate 10 gr., bismuth subgallate 20 gr., powdered alum 3 gr., boric acid 128 gr. Antiseptic dusting powder for wounds, eczema, etc.

**E.D.P.** (*Evans, Sons, Lescher & Webb, Liverpool*). Bismuth formic iodide as surgical dusting powder.

**Bismuthi Subnitrates** (*B.P.C., P. Ned V, P. Helv. V, P. Ital. V, P.G. VI, P. Dan., U.S.P. XI*). *Syn.* BISMUTH OXYNITRATE, MAGISTERIUM BISMUTHI.

*Dose* —5 to 20 grains (0.3 to 1.2 g.).

A white microcrystalline powder, containing 79 to 81% of  $\text{Bi}_2\text{O}_3$  (*P. Jap.* and *P. Ital.* 79 to 82%), obtained by precipitating a bismuth nitrate solution with alkali. Composition corresponds to  $6\text{Bi}_2\text{O}_3, 5\text{N}_2\text{O}_5, 9\text{H}_2\text{O}$ . The oxysalt,  $\text{BiONO}_3, \text{H}_2\text{O}$ , obtained by precipitation of bismuth nitrate solution with water, contains about 76% of  $\text{Bi}_2\text{O}_3$ .

*P. Jap.* gives method of making—i.e., bismuth 1, nitric acid (sp. gr 1.2) 5, dissolve and allow to crystallise, then take the crystals 1, water 4, and add boiling water 21. Pour off, wash with water 25, and dry at  $30^\circ$ .

**Incompatible** with alkaline carbonates, also decomposes potassium iodide, and incompatible with tannin and sulphur.

Best suspended in aqueous vehicle by compound tragacanth powder, 1 dr to 8 oz, or by powdered acacia or with half its weight of starch powder—*Pharm J*, 1/1926, 96.

**Uses.** In gastric ulcer and dysentery as an intestinal antiseptic, and occasionally as a dusting powder in eye work. During the war it was used with iodoform for wounds, in the form of "B I P P."

Gastric ulcer may be treated by bismuth subnitrate rubbed into a paste with liquid paraffin,—a good vehicle for bismuth, undoing its constipating effect. Decomposition into nitrite in the stomach is avoided *cf* Bismuth Carbonate.

As a dusting powder for wounds it has caused poisoning.

**HYPERTENSION.** Following the administration of bismuth subnitrate by mouth, the nitrite content of the blood is increased by three or four times the normal concentration. This increase in nitrite concentration is associated with a fall in the arterial tension. The nitrite content of the blood is likewise increased by sodium nitrite taken by mouth. The increase in concentration is of the same order of magnitude. Reduction of the arterial tension does not invariably follow taking bismuth subnitrate by mouth, but in such instances there is no increase in the nitrite content of the blood. Thus a parallelism between the nitrite content of the blood and the arterial tension has been shown. The experimental evidence confirms the clinical impression that following the oral administration of bismuth subnitrate, small amounts of nitrite are slowly and continuously absorbed from the bowel—E. J. Stieglitz and A. E. Palmer, *J. Pharmacol.*, 1936, 56, 222.

Bismuth subnitrate assists materially in obtaining a reduction of arterial tension, owing to breaking the vicious circle of vascular fatigue, hyperirritability, with more spasticity and fatigue, and thereby permitting of physiologic rest—E. J. Stieglitz, *J. Pharmacol.*, Dec, 1928, 422.

**SYPHILIS.**—Bismuth subnitrate as effective as any other bismuth compound. Good results with following injection. Bismuth subnitrate 10 g, Novocaine nitrate 1 g, sterile almond oil 100 g, the dose being 1 ml (0.07 g of bismuth) every third day—E. Sonnenberg, *per Prescriber*, 1926, 329.

**Enema Bismuthi et Sodii Salicylatis.**

Bismuth subnitrate 3 dr, sodium salicylate  $2\frac{1}{2}$  dr, psyllium seed mucilage to 1 pint.

**COLITIS,** the treatment of, by Revelliod's method (modified).

Empty the bowels by enemata of warm water twice daily for three days—on the fourth day inject the above. Action of the bowels must be discouraged.

after the injection, as the medicament should be retained for two days, if possible, to permit of absorption.

During the injection the patient should lie upon the left side with the pelvis raised 2 or 3 inches. This treatment has, of course, no effect upon enteritis alone or complicating (? originating) colitis; consequently a modification is necessary.

[D-P1-81] **Insufflatio Bismuthi et Morphinae (B.P.C.).**

*Syn.* FERRIER'S SNUFF.

Bismuth subnitrate 75% and morphine hydrochloride 0.4% in powdered acacia.

From 1 to 2 drachms may be used in 24 hours as snuff for catarrh. For acute coryza add powdered cubebs. It may cause drowsiness for some hours in susceptible patients.

**Injectio Bismuthi Subnitratis.**—BECK'S BISMUTH PASTE. For X-ray examination of fistulae (*cf.* also Bismuthi Subchloridum).

It sometimes causes toxic symptoms after application. If this occurs, remove dressing, wash out wound. Give morphine,  $\frac{1}{4}$  gr. hypodermically, if cramps in limb are severe.

(a) For DIAGNOSIS AND EARLY TREATMENT. Place bismuth subnitrate 1 in a mortar sterilised by burning a little spirit in it and add in portions hot melted white soft paraffin 2.

(b) For LATE TREATMENT. Bismuth subnitrate 6, white wax 1, hard paraffin 1 (m.p. 120°F.), white soft paraffin 12. Prepare on similar lines to the last.

The (a) form was originally injected to diagnose the extent of chronic tuberculous sinuses. It was found also to have curative effect. It is melted before use. The (glass) syringe must be sterilised dry and the plunger dipped in sterile oil before charging. —Beck, "Fistulous Tracts, Tuberculous Sinuses and Abscess Cavities."

The following is a modification:—Bismuth oxychloride 1, white soft paraffin  $1\frac{1}{2}$ , liquid paraffin  $1\frac{1}{2}$ , for injection into sinuses.

By X-ray examination, sinuses can be localised. Large quantities should not be left *in situ*.

Three ounces of (a) injected at the knee, and later 4 ounces further caused poisonous effects. Caution is necessary when using for diagnostic purposes.

The bismuth is bactericidal, chemotactic and astringent. Mechanical action is also good.

**Pasta Bismuthi et Iodoformi (B.P.C.).** *Syn.* B.I.P.P.

Bismuth subnitrate 25, iodoform 50, liquid paraffin 25 (by weight).

Large infected wounds have been treated without special drainage, the paste being applied as a thin covering over the wounded surface, which is then dressed in the usual way. Wounds can be closed by sutures at any period and the dressings can be left on one to six weeks.

**B.I.P.P. modified.**—Bismuth subnitrate 1, iodoform 2, and soft paraffin 13. Good in appendicitis operations, but some say should never introduce it into the abdomen.—R. A. Stoney, *Brit. med. J.*, ii/1930, 737.

POISONING in a girl of 8 following the use of 1 ml. of the paste after swabbing the wound with ether. Rapid pulse-rate, high temperature and dry skin,

vomiting, diarrhoea and delirium. Recovery after irrigations of wound with 10% sodium bicarbonate solution, glucose per rectum and salines intravenously. —R. C. Shaw, *Lancet*, i/1933, 250

**OSTEOMYELITIS** The more frequent use of "B.I.P.P." urged in treatment *Brit. med. J. Epit*, i/1926, 20.

**TROPICAL ULCER** well treated —T. R. E. Kerby, *Lancet*, i/1932, 237.

[D P1 81] **Unguentum Bismuthi cum Cocaina** (*St. Mark's H.*).

Bismuth subnitrate 120 gr., cocaine hydrochloride 8 gr., white soft paraffin to 1 oz.

**Bismocarbon** (*Richter, London*) Tablets contain bismuth subnitrate 4 gr and charcoal 4 gr. In dysentery, gastro-enteritis, etc.

**Bisodol** (*Bisodol, London*). Bismuth subnitrate, magnesium carbonate, sodium bicarbonate, carica papaya, diastase, oil of peppermint. *Dose*.—One level teaspoonful in water. Antacid

**Muthydral** (*Anglo-French Drug Co, London*) Tablets contain basic bismuth subnitrate 0.49 g., mercury subchloride 0.01 g. *Dose*.—2 tablets daily as auxiliary to other treatments or 4 tablets daily for 20 days in each month when no other treatment is given. Anti-syphilitic

**Bismuthi Tannas.** *Syn. and Prop.* TANNISMUT (*Heyden, Dresden; Braun, London*), BISMUTUM BITANNICUM, (*P. Helv. V*).

*Dose*.—5 to 30 grains (0.3 to 2 g.).

A brownish-yellow powder insoluble in water. Is astringent, and useful in diarrhoea and dysentery.

## BROMUM

*B.P.C.*

Br = 79.9.

A dark brown liquid, sp. gr. about 3.14, with penetrating odour. Soluble 1 in 30 of water *w/w*; readily soluble in organic liquids with gradual decomposition of the solvents. Is not used as such medicinally. Since the war bromine has been made in large quantities in France from sea water.

**Antidotes.** Emetics sometimes useful. Inhalations of very dilute ammonia, also of alcohol. Keep patient in fresh air. Give milk, white of egg or starch mucilage. Steam inhalations sometimes useful. Oxygen inhalations. Atropine, 10 gr., hypodermically. Venesection and blood transfusion may be necessary.

**Bromal Hydras.**  $\text{CBr}_3 \cdot \text{CH}(\text{OH})_2 = 298.8$ .

*Dose*.—2 to 5 grains (0.12 to 0.3 g.) at bedtime.

In large colourless crystals, which melt on the hand, soluble in water 1 in 2½. Applied externally it irritates the skin. It has been tried in epilepsy, chorea and insomnia.

**Brom-Albumen.** *Syn.* BROMO-PROTEIN.

*Dose*.—10 grains (0.6 g.) = ¼ gr. of bromine approx.—increased as desired

Contains 7% of bromine, combined with albumen. Made by interaction of bromine with egg albumen, in form of a light brown powder. As a substitute for alkali bromides in epilepsy, where larger doses than the above may be required. It is hardly soluble

in 0.2% hydrochloric acid, even in presence of pepsin, but is readily dissolved in 0.5% sodium bicarbonate in the presence of pancreatin, hence absorption takes place in the intestines

**Bromlecthin** (*Richter, London*) Natural lecithin containing 20% bromine in tablets Neurasthenia

**Brominoleum** (*Martindale, London*). *Syn.* BROMINOL (33%)

*Dose.*—10 to 60 grains (0.6 to 4 g.), approximately equivalent in content of bromine to 5 to 30 gr. of potassium bromide.

An additive compound of bromine and sesame oil, containing 33½% of the halogen in form of a thick brown odourless oil; sp. gr. 1.31. Gradually liberates bromine to the system

*Uses.* In epilepsy and all forms of nerve trouble, also in headache and sea-sickness. May also be rubbed into the skin if diluted with an equal weight of lanolin ointment.

It may be taken internally shaken up with an equal volume of syrup, in beer, wine or milk, or dispensed as follows. Brominol 33% 2 oz., acacia 1 oz., chloroform 18 drops, rub together and add quickly with vigorous agitation water q.s. to 6 oz. *Dose*—2 drachms, equal 20 gr. of potassium bromide

**Brominol** containing 10% of bromine is also prepared.

A dose of ½ ounce of this equals approximately 20 grains of potassium bromide. Sp. gr. 1.045

[P1] **Mistura Brominol cum Nuce Vomica.** Brominol 30 gr., acacia 30 gr. tincture of nux vomica 6 m., spirit of chloroform 15 m. water to ½ oz. For one average dose

**Bromipin** (*Merck, Darmstadt, Martindale, London*) Addition product of bromine and sesame oil, in two strengths, 10% and 33½%. Tablets correspond to 0.4 g. of bromine or 0.6 g. of potassium bromide

**Multibral** (*Napp, London*) Sodium monobromoleate. Coated pellets contain 0.03 g. of bromine. *Dose.*—1 to 3 pellets thrice daily. For intensified bromine action with freedom from secondary effects

**Bromoformum** (*B.P.C., P. Helv., V, Fr. Cx., P. Ital. V, P. Ned. V, P. Belg. IV, F.E. VIII*) *Syn.* TRIBROMOMETHANE CHBr3 = 252.8.

*Dose*—½ to 2 minims (0.03 to 0.12 ml.) or more. *P.G. VI* and *Fr. Cx.* have maximum single dose 0.5 g.; maximum during 24 hours 1½ g. (= 8 minims approx.) Children as many drops as years old—up to 6

A heavy, limpid, colourless, sweet liquid, with an agreeable odour; sp. gr. about 2.63. Distils mainly between 148° and 155°

**Soluble** 1 in 800 of water, 1 in 80 of glycerin. Miscible with alcohol 90%, chloroform, ether and fixed and volatile oils. It should be preserved by addition of 0.5 to 1% alcohol. Is a powerful sedative, useful in insane cases. Capsules contain ½ minim (0.03 ml.) dissolved in oil.

**Aqua Bromoformi.** Well shaken, 1 minim is dissolved in 2 ounces of water.

*Dose.*—1 to 4 ounces (30 to 120 ml.).

For sea-sickness half doses occasionally.

**Elixir Bromoformi** (*B.P.C.*). *Syn.* MISTURA BROMOFORMI COMPOSITA.

*Dose.*— $\frac{1}{2}$  to 2 drachms (2 to 8 ml.).

Bromoform 1 in 50, with alcohol 90%, tincture of orange, compound tincture of cardamom and glycerin.

### **Syrupus Bromoformi.**

*Dose.*— $\frac{1}{2}$  to 1 ounce (8 to 30 ml) =  $\frac{1}{2}$  to 2 minims of bromoform. To be diluted with an equal quantity of water or more, at time of taking.

Bromoform 2 m., alcohol (90%) 80 m, syrup 160 m., glycerin  $\frac{1}{2}$  oz.

The Sirop of the *Fr. Cx. Supp.* 1926 is bromoform 1, alcohol (90%) 9, glycerin 30, syrup 160.

**Uses.** In whooping cough diminishes number, duration and severity of attacks, and mucous secretion is more easily got rid of.

### [P1] **Syrupus Bromoformi Compositus (B.P.C.).**

*Dose.*—1 to 4 drachms (4 to 16 ml.).

1 dr. contains about  $\frac{1}{17}$  m. of bromoform,  $\frac{3}{16}$  gr of codeine and  $\frac{1}{8}$  m. of tincture of aconite.

### [P1] **Syrupus Bromoformi Compositus (P Ital V)**

20 g contains 0.02 g of bromoform, 0.01 g of codeine, and 0.04 g of aconite tincture

[P1] **Rami Syrup (Fougerat, Paris)** *Dose*—Adult, 1 tablespoonful 3 to 5 times a day Children over 5, 1 teaspoonful 3 to 5 times daily. Children under 5, 15 minims diluted, every hour or  $\frac{1}{2}$  hour according to age *Contains "per (tablespoon) dose"* Alcoolature d'Aconit 3 drops, codeine 0.01 g, bromoform 2 drops, tolu 0.05 g

**Brometone (Parke, Davis, London)** TRI-BROM-TERTIARY BUTYL ALCOHOL  $C_4H_9OBr_3 = 310.8$  *Dose*—5 grains (0.3 g), repeated 2 or 3 times during 24 hours

White crystals melting at 167° containing about 77% of Br. **Soluble** in alcohol, slightly in cold water. Hypnotic, analgesic, antiseptic. Useful in sea-sickness.

In epilepsy, in some cases, of value and has some hypnotic power.

Large doses may produce dizziness, loss of appetite, and mental heaviness

**Capsules of Brometone**, 5 grains in each.

**Avertin (Bayer Products, London).** *Syn.* TRIBROMETHYLALCOHOL or E.107  $CBr_3CH_2OH = 282.8$ .

[P1] "*Tribromethyl alcohol.*"

[S1] "*Tribromethyl alcohol.*"

An anæsthetic, stated to have been first made by reduction of bromal (1926). It is the subject of German Patent 437,160. White crystals containing 85% of Br.

**Soluble** 3 in 100 of water at 37°.

It is available as a solution in amylene hydrate containing 1 g. of tribromethyl alcohol in 1 ml. This solution (**Avertin Fluid**) is miscible with water.

*Dose.*—0.1 g. per kilo is safest, but for exhausted patients whose glycogen reserves are diminished and powers of detoxicating Avertin are impaired, 0.08 g. Maximum dose, apart from weight, 10 g. The solution is administered in 2.5 to 3% aqueous solution per rectum (by gravity). It is non-irritant to the mucosa. Surgical anæsthesia can be superimposed. Solutions must be made without heat.



**Reaction of the solution** must be determined by adding 2 drops of 1 in 1000 solution of Congo red to 5 ml of Avertin solution. The orange colour should be unchanged.

Universal Indicator is a more sensitive and reliable agent as a test for the purity of Avertin solution. Transfer 3 mg of prepared Avertin to a clean test tube, and cool. Place in a similar test tube an equal volume of the distilled water used in the preparation of the Avertin solution. Add 2 drops of Universal Indicator to the contents of each tube. The colour of the Avertin solution should be greenish-yellow and it should not be possible to detect any difference in colour between the two tubes. Avertin solution should never be prepared at a temperature exceeding 40° and should be kept in a bottle rather than a vacuum flask prior to administration, which should be not later than one hour after its preparation.—H. K. Ashworth, *Brit. med. J.*, ii/1933, 489. See also W. H. Butchers, K. Bullock and G. R. Priddey, *Quart. J. Pharm.*, 1933, 532.

The combination of Avertin with  $\frac{1}{2}$  grain morphine and  $\frac{1}{2}$  grain hyoscine is a highly dangerous procedure.—R. Blair Gould, *Brit. med. J.*, i/1934, 400.

**Contraindications.**—Contraindicated in renal disease—no adequate margin of safety between surgical anaesthesia and death.—J. R. Veal and co-workers, *J. Pharmacol.*, 1931, 643.

Complete Avertin anaesthesia is contraindicated in very young and very cachectic children.—J. Boyd, *Brit. med. J.*, i/1935, 1122.

**Toxic effects.**—Decomposition products formed by the action of heat (over 50°), light, and air are irritant to the rectal mucosa. In anaesthetic doses it has no effect on the cardio-vascular system, but in larger doses it slows the rate and weakens the force of the heart-beat—coronary vessels dilate and blood pressure falls. Toxic doses cause death by respiratory paralysis. It is excreted in the urine over a period of several days—more than 50% in the first 24 hours.—F. B. Parsons, *Brit. med. J.*, ii/1929, 712. See also G. Edwards, *ibid.*, 713.

No great change occurs in the patient for 10 to 15 minutes after the dose. Respiration then becomes slow and shallow, and slight cyanosis may be noticed.—F. B. Parsons, *Brit. med. J.*, ii/1930, 554.

**Antidotes.**—As an antidote for overdose high rectal irrigation with warm hypertonic sodium thiosulphate solution acts as restorative if applied before cardiac failure occurs.—A. Bollinger, per *Lancet*, i/1932, 944.

Respiratory failure and cardiac embarrassment occurring with this narcotic never fail to respond to administration of carbon dioxide, with or without oxygen.—A. Barnsley, *Brit. med. J.*, i/1934, 456.

Narcosis averted by Coramine 2 to 3 ml intramuscularly.—W. P. Kennedy, *Lancet*, i/1932, 1143.

**BASAL ANÆSTHESIA**—For reduction of fractures, in combination with local anaesthesia it is ideal.—B. Hughes, *Brit. med. J.*, i/1929, 898, *Lancet*, ii/1929, 1220.

Used 2½ years in combination with other drugs, themselves not anaesthetics but rather amnesics, with big fall in mortality rate.—B. Hughes, *Brit. med. J.*, ii/1930, 887.

Where there is serious pulmonary disease, Avertin advised, in combination with local anaesthetic or gas and oxygen it is said to be ideal.—Sir F. E. Shipway, *Brit. med. J.*, ii/1930, 663.

As a basal hypnotic, per rectum, 0.1 g. per kilo in 2.5% solution.—I. W. Magill, *Lancet*, i/1931, 353. Preferable to paraldehyde, especially for children.—Sir F. E. Shipway, *ibid.*, 354. Valuable in ear, nose, and throat operations.—Sir J. Dundas-Grant, *ibid.*

**GENERAL ANÆSTHESIA**—In only 40 to 50% of cases is full anaesthesia assured by its use alone. Liquid diet only to be given the night before operation. Narcosis lasts 2 to 4 hours. Of value in operations on thorax and upper respiratory tract and in cranial surgery.—*Brit. med. J. Ept.*, i/1928, 3.

Avertin can be given to children as a complete anaesthetic with safety, and approaches more nearly the ideal anaesthetic than any other. It is better than basal anaesthesia followed by inhalation anaesthesia, and is safer in children than adults. The best method is to combine 0.175 g. per kg. body weight with morphia and atropine according to age and 20 to 30 ml. of Novocain as a field block. A 3% solution of Avertin is better retained than a 2½%. The fall in blood pressure is not of serious moment.—J. Boyd, *Brit. med. J.*, i/1935, 1122.

**GYNECOLOGY**—A safe drug in a dosage of 0.08 to 0.1 g. per kilo. 2000 gynaecological operations conducted without mortality or morbidity traceable to its use. Reduction of pre-anæsthetic morphine from  $\frac{1}{4}$  to  $\frac{1}{8}$  grain resulted in immediate lessening of respiratory depression—J. Young and N. S. Fraser, *Brit. med. J.*, 1/1934, 455.

**OBSTETRICS**—In childbirth advocated for safety, ease of administration, and mitigation of pain. It is given at second stage pains after morphine  $\frac{1}{4}$  grain at first (sometimes a further  $\frac{1}{8}$  grain). There must be 2 hours' interval between morphine and Avertin. Should be given when the cervix is fully half dilated, if the contractions are strong and regular. Some excitement may follow for 5 minutes. *Dose*—0.075 ml. *Avertin Fluid* per kilo weight, e.g., 4.5 ml. for a person of 9 stone (60 kilos), given per rectum in 1000 ml. warm water—milk has been used in preference—Prof. Martin. The method eases pains of labour.—J. S. M. Connell, *Lancet*, 11/1930, 184.

Pleasant for the patient. Harmless to the infant. Not dangerous, but uncertain in action. More experience required to compare its merits with paraldehyde—Gertrude M. B. Morgan, *Brit. med. J.*, 11/1932, 12.

## BUCHU

(with AGROPYRUM, etc.)

### B P

The dried leaves of *Barosma betulina* (Rutaceæ), contain volatile oil and mucilage. Carminative and diuretic. Buchu has antiseptic action in irritability of bladder and in gonorrhœa.

#### **Extractum Buchu Liquidum (B.P.C.).**

*Dose*—5 to 20 minims (0.3 to 1.2 ml.) 1 in 1.

#### **Infusum Buchu Concentratum (B.P.).**

*Dose*—1 to 2 drachms (4 to 8 ml.) 1 in 2½.

#### **Infusum Buchu Recens (B.P.).**

*Dose*—1 to 2 ounces (30 to 60 ml.) 1 in 20.

In preparing this the leaves must be lightly broken and not bruised, otherwise percolation is prevented by the mucilage—B. A. Bull, *Pharm. J.*, 1/1932, 318.

#### **[P.] Mist. Buchu et Hyosc. (N.I.F.)**

Potassium bicarbonate 15 gr., liquid extract of hyoscyamus 3 in., concentrated infusion of buchu 15 m., chloroform water to  $\frac{1}{2}$  oz.

**Tinctura Buchu (B.P.C.)** *Dose*— $\frac{1}{2}$  to 1 drachm (2 to 4 ml.) 1 in 5.

**Agropyrum (B.P.C., P. Helv. V.)** *Syn.* COUCH GRASS. The dried rhizome of *Agropyron repens* (Gramineæ). Contains triticin, a carbohydrate similar to inulin. Diuretic and aperient. Useful in gonorrhœa.

**Decoctum Agropyri (B.P.C.).** *Syn.* DECOCTION OF TRITICUM.

*Dose*— $\frac{1}{2}$  to 2 ounces (15 to 60 ml.) 1 in 20.

**Extractum Agropyri Liquidum (B.P.C.)** *Syn.* LIQUID EXTRACT OF TRITICUM.

*Dose*—1 to 2 drachms (4 to 8 ml.) 1 in 1.

**Ammi Visnaga.** *Syn.* KHELLA. The fruits of *Ammi Visnaga* have diuretic properties. Preparations relax all smooth muscle, and have been given in ureteric spasm and to assist the passage of small kidney stones. Has been administered as a decoction (1 in 40, *dose*— $\frac{1}{2}$  to 2 oz.) and as a tincture (1 in 10 by maceration in alcohol 90%, *dose*—1 to 3 dr.), given thrice daily before food.

Activity is due to a crystalline principle, visamin.—K. Saman, *Quart. J. Pharm.*, 1932, 16. See also *ibid.*, 1930, 25; 1931, 14, 1932, 186.

**Chimaphila** (B.P.C.). *Syn.* PIPSISSEWA.

*Dose.*—15 to 45 grains (1 to 3 g.).

The dried leaves of *C. umbellata* (Pyrolaceæ). Has diuretic properties, and is used in cardiac and renal disease, being administered as Extractum Chimaphilæ Liquidum, 1 in 1, either alone or mixed with 3 parts of syrup.

**Lappa** (B.P.C.) *Syn.* BURDOCK.

Roots of *Arctium majus*, or other species of *Arctium*. Has diuretic, diaphoretic and alterative properties. On the Continent called Bardana, e.g., *Inf. Bardanæ Spirituos* (external). Bardana 2, water (boiling) q.s. to 15, strong alcohol 5, to be rubbed into the scalp. Liquid extract 1 = 1 by diluted alcohol. *Average dose.*—30 minims. Decoction, 1 in 20. In skin affections and gout.

The use of a tincture of the seeds has largely replaced that of the root in U.S.A., especially in the treatment of psoriasis, acne and prurigo—*Chem & Drugg*, 1/1925, 216.

**Maidis Stigmata** (*P. Helv. V*) *Syn.* CORN SILK

The dried stigmas and styles of maize, *Zea Mays* (Gramineæ). Demulcent and diuretic. Used in cystitis and nocturnal incontinence of urine.

**Extractum Maidis Liquidum.** *Dose*—1 to 2 drachms 1 in 1

**Syrupus Maidis.** *Dose*— $\frac{1}{2}$  to  $\frac{1}{2}$  drachm. Liquid extract 1, syrup 9

**Uva Ursi** (B.P.C.). *Syn.* BEARBERRY LFIVES, BUSSESOLE (*Fr. Cx., P. Dan.*).

The dried leaves of *Arctostaphylos Uva-ursi* (Ericaceæ). Contains a crystalline glycoside, arbutin,  $C_{12}H_{16}O_7, \frac{1}{2}H_2O$ , m.p. about 168°. Bearberry is diuretic and astringent and exerts an antiseptic effect on the urinary tract. It is employed in urethritis, cystitis, etc.

**Infusum Uvæ Ursi Concentratum** (B.P.C.) 1 in 2 $\frac{1}{2}$  *Dose*— $\frac{1}{2}$  to 1 drachm (2 to 4 ml.).

**Infusum Uvæ Ursi Recens** (B.P.C.). *Dose*— $\frac{1}{2}$  to 1 ounce 1 in 20

## BUGINARIA

Bougies are medicated pencils intended for insertion into the urethra, nostrils or ears. They are prepared in the same way as suppositories but differ in shape, resembling a pointed rod.

**Urethral Bougies** are usually in two sizes: (a) 2 $\frac{1}{2}$  inches and weighing 15 gr., or (b) 5 inches and weighing 40 gr. They have about the diameter of a No. 8 or No. 9 catheter respectively. If the size is not specified by the prescriber, it is usual to supply the smaller size. Metal moulds can be obtained to give these sizes.

The basis may be either gelato-glycerin or oil of theobroma. A suitable gelato-glycerin base may be prepared from the following formula:—Gelatin 32.5 g., glycerin and water of each 40 ml. Incorporate and evaporate to 100 g. Bougies made with this basis are directed to be dipped in warm water prior to insertion. When prepared with theobroma basis, bougies may be made by

other methods than moulding. Thus the medicament may be incorporated in the basis by massing in a pill mortar, afterwards piping the mass on a pill machine and shaping one end with the fingers. If this method is adopted it may be advisable to incorporate about 5 to 10% of wool fat. Lubricated glass tubing of suitable diameter may be used as a bougie mould, the melted mass being sucked up into it, allowed to solidify, then pushed out with a glass rod and cut to the correct length, one end being subsequently pointed. Urethral bougies are sometimes known as *cereoli*.

**Nasal Bougies** are usually made with a gelato-glycerin basis, and resemble the small size urethral bougie in size and shape.

**Aural Bougies** are made with a gelato-glycerin basis unless otherwise ordered. They are usually  $\frac{1}{2}$  inch in length, and weigh about 6 gr. Bougies for the ear are sometimes known as *aurinaria*.

## CAFFEINA

*B.P., U.S.P. XI, P.G. VI, P.Ned. V, Fr. Cx., P.Jap., P.Ital. V, P.Helv. V, P.Dan., F.E. VIII, P.Belg. IV.*



*Syn.* THEINE, GUARANINE.

*Dose*—2 to 5 grains (0.12 to 0.3 g.) or more—as much as 18 grains being recommended—given in solution, or in pills.

A crystalline alkaloid, m.p. about  $235^\circ$  to  $237^\circ$  after drying at  $100^\circ$ , usually obtained from the dried leaves of *Camellia Thea*, or dried coffee-seeds—*Coffea arabica*, also contained in guarana, maté and kola. Caffeine and theobromine (*qv*) can be prepared from xanthine (theobromine being di- and caffeine tri-methyl-xanthine). These are purine derivatives.

**Soluble** 1 in 80 of water, about 1 in 40 of alcohol 90%, less in ether, acids render it more soluble in water, but it is a feeble base, and on concentrating the solution of the salts they are apt to split up, and the caffeine crystallises out by itself. Is rendered soluble in less water by the addition of an equal quantity of phenazone, sodium salicylate, etc. *See also* Caffeine-Sodio-Salicylate, etc.

**Antidotes.** Empty stomach by emetic or by stomach tube, using 60 gr. of potassium permanganate in 2 gallons of water. Give brandy,  $\frac{1}{2}$  oz., or aromatic spirit of ammonia,  $\frac{1}{2}$  dr., in water freely. Keep patient warm, especially extremities. Morphine,  $\frac{1}{2}$  gr., with atropine  $\pi\text{h}$  gr. hypodermically.

**Uses.** In heart affections (*eg*, cardiac failure in pneumonia), but its power as a cardiac stimulant is doubted, nervous headache, dropsy (of value in renal dropsy), and as a stomachic (lessens metabolism). It wards off fatigue. Also given in diarrhoea. Subcutaneously in rheumatic affections with sodium salicylate, *qv*. Applied to the eye, it dilates the pupil,

Bronchial asthma of adults is relieved by 2 to 5 grain doses of the citrate before bedtime and again during the night.—Yeo

*Neuralgic Powders.* Caffeine 1 gr., quinine hydrochloride 5 gr., phenazone 10 gr. (or phenacetin 5 gr.).

Drugs of the caffeine series have a most complex effect on the circulation of animals. They tend to raise blood pressure by stimulating the vasomotor centre, tend to lower it by dilating peripheral vessels, and also cause tachycardia through direct action on the heart muscle. In man, the net results are remarkably slight and inconstant, indeed, one of us, working with the late Prof. Cushny some years ago, found no demonstrable effects upon either the pulse rate or blood pressure of patients from even intravenous injections of caffeine citrate in ordinary doses. Such evidence shows how slight is the foundation for the wide belief in its virtues as a circulatory stimulant.—C. Hoyle and J. W. Linnell, *Practitioner*, 1/1936, 96.

**Elixir Caffeinæ (Martindale)**

*Dose.*—1 to 2 drachms (= 1 to 2 grains of caffeine) Caffeine 17.5, dilute hydrobromic acid 4, simple elixir to 1000

**[P1] Elixir Antineuralgicum.**

*Dose.*—1 to 2 drachms (4 to 8 ml)

Phenazone 50, caffeine 30, cocaine hydrochloride 1, cochineal tincture 6, elixir of orange 25, alcohol (75%) to 1100. Has been used on the Continent for headache

**Tabellæ Caffeinæ (B.P.C.)** contain 1 gr. (0.06 g.).

**[P1] Caffeine-Chloral.**

Small white granular crystals, freely soluble in water, with the taste of chloral. Is analgesic and laxative, and in hypodermic injections of 3 to 8 grains useful in constipation, painful gastric distension, sciatica, and rheumatism

**Caffeinæ Citras (B.P.C., P. Helv. V, F.F. VIII)**

$C_8H_{10}O_2N_4 \cdot C_3H_7(OH)(COOH)_3 = 386.2$  *Syn* CAFFEINA CITRATA (U.S.P. XI).

*Dose.*—2 to 10 grains (0.12 to 0.6 g.).

A white odourless powder obtained by combining caffeine 1 and citric acid 1 in a small quantity of distilled water and evaporating to dryness on a water bath

**Soluble** 1 in 4 of hot water, dissociating on further dilution, with separation of caffeine, which re-dissolves in 32 of water; 1 in 22 of alcohol 90%.

**Incompatible** with potassium iodide and Spiritus Ætheris Nitrosi, iodine being liberated. The following, however, does not darken:—Potassium iodide 5 gr., caffeine base 2½ gr., Spiritus Ætheris Nitrosi (neutralised with ammonium carbonate) 30 m., water to 1 oz.

Also incompatible with sodium salicylate. A little sal volatile or sodium hydroxide will prevent the salicylic acid being thrown out—or use half the citrate as caffeine base

**Uses.** See Caffeine.

**Caffeinæ Citras Effervescens (B.P.C.).**

*Dose.*—1 to 2 drachms (4 to 8 g.).

Contains 4% of the citrate, or about 2½ grains in a drachm.

**Caffeina et Sodii Benzoas (B.P.).** *Syn* CAFFEINÆ SODIO-BENZOAS (P. Jap. IV, P.G. VI, U.S.P. XI, P. Belg. IV, P. Ital. V, P. Helv. V, P. Dan.).

*Dose.*—5 to 15 grains (0.3 to 1 g.); 2 to 5 grains (0.12 to 0.3 g.) by injection, usually hypodermically. U.S.P. XI average doses 5 grains and 3 grains respectively.

Contains from 47 to 50% of caffeine. *P. Ned. V* requires 50%; *P. Ital. V* must yield 43 to 46% of anhydrous caffeine.

**Soluble** 1 in 4 of water, 1 in 40 of alcohol 90%. Warm water dissolves about 1 in 1, but caffeine separates on cooling.

As stimulant for desperately ill patients 2 grain doses, *intravenously*. It improves breathing, circulation and other fundamental functions, and, following its use, the mind and depressed vital reflexes become active and normal. Coma, shock, collapse under anaesthesia, and poisoning from morphine and other depressant drugs treated.—W. W. Duke, *J. Amer. med. Ass.*, 1/1923, 998, see also *Pharm. J.*, 1/1923, 403.

**HÆMOGLOBINURIC FEVER** well treated with caffeine sodio-benzoate intramuscularly, 3 grains twice daily for 7 days and once daily for further 5 days.—A. A. Facio and M. D. Rojas, *J. trop. Med. (Hyg.)*, 1925, 88.

**SHOCK**—For use in the event of severe Novocain reaction. Caffeine 3 gr., sodium benzoate 7 gr., strychnine  $\frac{1}{10}$  gr.—C. Hope Carlton, *Brit. med. J.*, 1/1925, 651.

[P1] **Labat's Cardiac Stimulant** (*Anglo-French Drug Co., London*).

Caffeine 0.25 g., sparteine sulphate 0.05 g., sodium benzoate 0.30 g., strychnine sulphate 0.001 g., distilled water to 2 ml. For counteracting fall of blood pressure during regional anaesthesia.

**Caffeinæ et Sodii Salicylas** (*B.P.C., P. Helv. V, P. Dan.*)  
*Syn.* CAFFEINÆ SODIO-SALICYLAS.

**Dose.**—2 to 5 grains (0.12 to 0.3 g.) hypodermically, or 5 to 15 grains (0.3 to 1 g.) orally. Max. single dose *per os* 1 g., or in 24 hours, 3 g.

Evaporate to dryness caffeine 50, sodium salicylate 50, water sufficient to form a smooth paste. A white amorphous powder, containing 47 to 50% of caffeine.

**Soluble** 1 in 1 of water, 1 in 28 of alcohol 90%.

The addition of camphor to injections of caffeine sodium salicylate has been suggested. Thus to 3 ml. of pure sterile glycerin add a solution of caffeine and sodium salicylate of each 0.25 g. in water 1 ml.; then add spirit of camphor (10%) 1 ml.; 5 ml. contain caffeine 0.25 g., and camphor 0.1 g.

This salt and the corresponding cinnamate and benzoate act like digitalis, but more rapidly.

Iritis of rheumatic origin has been treated by injection into the median cephalic vein of caffeine 0.05 g. with sodium salicylate 0.5 g.

**Caffeinæ Hydrobromidum** (*B.P.C.*).

$C_8H_{10}O_2N_4 \cdot HBr \cdot 2H_2O = 311.1$ .

**Soluble** 1 in 50 approx.

The hydrochloride,  $C_8H_{10}O_2N_4 \cdot HCl \cdot 2H_2O = 266.6$ , and the hydriodide (unstable) are in use.

**Dose of each.**—1 to 4 grains (0.06 to 0.25 g.) or more. In transparent crystals.

**Effervescent Caffeine Hydrobromide** is prepared containing 4%, or about  $2\frac{1}{2}$  grains in a drachm.

**Dose.**—1 to 2 drachms (4 to 8 g.).

**Caffeinæ Iodidum.** *Syn.* CAFFEINÆ TRI-IODIDUM, CAFFEINE DI-iodo-HYDRIODIDE.  $C_8H_{10}O_2N_4 \cdot I_2 \cdot HI \cdot H_2O = 593.9$ .

**Dose.**—1 to 3 grains (0.06 to 0.2 g.).

In prismatic black iridescent crystals, slightly soluble in water (with decomposition) and in alcohol 90%

Has been used with success in rheumatism and gout

[P1-81] **Pilula Caffeinae Tri-Iodidi Composita** (*Billumoria*)

*Dose*.—1 early in the morning, 1 about 3 or 4 p.m., and 1 at bedtime with water, to be lessened to 2 or 1 a day as required

Caffeine tri-iodide 2 gr., sodium aminarsonate  $\frac{1}{2}$  to  $\frac{1}{4}$  gr., valerianic acid 2 m., green extract of belladonna  $\frac{1}{2}$  to  $\frac{1}{4}$  gr., jalap extract, *q.s.* (if constipated), reduced iron 1 gr. (in asthma only) For one pill or preferably gelatin capsule

Asthma in India has been well treated with this compound

R. B. Billumoria (Bombay) states the majority of the cases there have not the usual book type "attacks," but dyspnoea during several nights, while during the day the patient is usually fairly comfortable, although the dyspnoea may be better or worse

Whooping cough, even in infants, with proportionately smaller doses, has likewise been well treated by this preparation

**Iodo-Caffeine** *Syn* SODIUM-CAFFEINE IODIDE, CAFFEINE SODIUM IODIDE.

*Dose*.—2 to 10 grains (0.12 to 0.6 g.).

A white powder, slightly soluble in cold water, freely in warm. Contains 65% of caffeine. Is a good diuretic, especially to prolong the diastole in cases of enfeebled heart. Is useful in cardiac dropsy, and pleurisy with effusion. Said not to disorder digestion.

**Elixir Caffeinae Iodidi** (*B.V.H.*) *Syn* CAFFEINE

Caffeine sodium iodide 5 gr., sodium iodide 5 gr., dilute hydriodic acid 5 m., decoction of coffee (3 oz. in 1 pint) 40 m., water to 1 dr. Given in asthma.

**Elixir Ephedrinae et Caffeinae** (*B.V.H.*) *Syn* EPICAFFEINE.

Is the same as the above, containing also  $\frac{1}{2}$  gr. of ephedrine hydrochloride per drachm

**Eupinal** (*Cuxson Gerrard, Oldbury*) Preparation containing iodide of caffeine for use in the treatment of asthma

**Eupnine Vernade** (*Darrasse, Nanterre, Wilcox, Jozeau, London*). Stable standardised solution of caffeine iodide (1 dr. = 0.5 g.)

*Dose*.—1 teaspoonful 2 or 3 times daily before meals. Asthma, emphysema and arteriosclerosis

**Spiroline** (*British Drug House, London*). Elixir containing in each drachm 3 gr. of di-iodo-caffeine hydriodide with the soluble constituents of  $7\frac{1}{2}$  gr. of coffee. In asthma and as a cardiac stimulant.

**Caffeinae Salicylas.**  $C_8H_{10}O_2N_4, C_6H_4OH \cdot COOH = 332.2$

*Dose*.—1 to 5 grains (0.06 to 0.3 g.).

White crystalline powder slightly soluble in water. Useful in migraine associated with rheumatism.

**Caffeinae Valerianas.**  $C_8H_{10}O_2N_4 \cdot C_5H_{10}O_2 = 296.2$ .

*Dose*.—1 to 3 grains (0.06 to 0.2 g.). In irregular crystals or powder, of somewhat variable constitution, usually consisting of a mixture of caffeine and valerianic acid, preferably in the proportion of 4 parts to 1. It controls hysterical symptoms, and is useful in pertussis.

**Catha Edulis.** *Syn* KAT, KHAT, ARABIAN or ABYSSINIAN TEA.

*Dose*.—1 drachm to  $\frac{1}{2}$  ounce (4 to 15 g.) infused in about 6 to 8 ounces of hot water as required. A sprig of about 10 leaves weighing about 10 grains is chewed at a time by natives.

The shrub grows wild in Abyssinia and is cultivated for native use in Arabia.

Three alkaloids were isolated by Stockman—*Cathine* (*d*-nor-isoeophedrine), very soluble in water, *cathinne* (less soluble) and *cathudine* (insoluble). In man they all act chiefly on the cerebrum and spinal cord, causing stimulation or much excitement according to dose, and cathine alone induces slight drowsiness at first.

The herb is a stimulant narcotic. It has been known for generations for its sustaining power. The leaves when used in an infusion in the same manner as tea or coffee, or when chewed (as by the Arabs), are stated to increase "staying power," and produce wakefulness and refreshment.

**Extractum Cathæ.** Dose— $2\frac{1}{2}$  to 10 grains (0.18 to 0.6 g.) A solid extract made with 60% alcohol, 1 = 4 of leaves.

**Extractum Cathæ Liquidum.** Dose—1 to 5 minims (0.06 to 0.3 ml.) Strength 2 = 1, prepared with alcohol 60%.

**Guarana** (*B.P.C.*, *P. Helv. V.*, *P. Hung.*)

Dose.—10 to 60 grains (0.6 to 4 g.) in powder, or infused in a cup of boiling water

The seeds of *Paullinia Cupana* (Sapindaceæ), roasted and moistened with water, made into a hard paste, rolled into cylinders, and dried. Imported from Brazil. The drug contains 2.5 to 5% of caffeine (guaranine), together with tannin, gum, etc. Is recommended for sick headache. A nervine tonic.

**Elixir Guaraniæ** (*B.P.C.*) Dose— $\frac{1}{2}$  to 2 drachms (2 to 8 ml.) Contains 80% v/v of tincture of guarana flavoured with cinnamon

**Tinctura Guaraniæ** (*B.P.C.*) Dose—1 to 2 drachms (4 to 8 ml.) 1 in 4

**Kola** (*B.P.C.*, *P. Helv. V.*)

Dose—15 to 45 grains (1 to 3 g.)

Seeds of *Cola vera* (Sterculiaceæ), containing about 1½% of caffeine and traces of theobromine

*Fr. Cx. Supp.* 1920 allows seeds of other varieties of *Cola* providing they contain at least 1.25% caffeine. (Not mentioned in *Fr. Cx. Supp.* 1926.)

**Extractum Kolæ Liquidum** (*B.P.C.*)

Dose.—10 to 20 minims (0.6 to 1.2 ml.) 1 in 1.

*Fr. Cx.* standardises to 1.25% of caffeine, but the method of manufacture is stated to be impracticable.

The administration of kola, coca and arsenic flavoured with a little elixir of orange forms a useful tonic and pick-me-up.

[P1] **Syrupus Kolæ Compositus** (*Martindale*).

Dose—1 to 2 drachms (4 to 8 ml.) twice daily.

Iron, quinine and strychnine citrate 3, citric acid 0.3, sodium glycerophosphate 5, liquid extract of kola 50, alcohol 90% 5, syrup of orange to 100. Finished product to be slightly acid. In anorexia, and as a general "tonic."

**Tinctura Kolæ** (*B.P.C.*)

Dose— $\frac{1}{2}$  to 1 drachm (1 to 4 ml.) 1 in 5.

**Vinum Kolæ** (*Martindale*).

Kola in coarse powder 1, in sherry 25, macerate for 7 days, filter and flavour with essence of vanilla

[P1-81] **Revitone** (*Hoffmann-La Roche, London*). Contains per oz. "Ext. Kola glycerin sacch." (= Sem. Kolæ 88 gr.), "Arsylen" brand of sodium allylarsenate 0.44 gr., dried extract of nux vomica 0.28 gr., sodium acid phosphate 16.22 gr., manganese chloride 0.09 gr. Dose.—1 or 2 teaspoonfuls 3 times daily. General tonic.



**Maté.** *Syn. and Prop. Name.* YERBA, PARAGUAY TEA, JESUIT TEA, HERVEA (*H. J. Lee, London*). The dried leaves of *Ilex paraguayensis* (Ilicaceæ). Contain 0.2 to 2% of caffeine. Is less astringent than tea and has none of the after-effects. Is tonic, laxative, febrifuge, and stimulant to the digestive organs

## CALCIUM

Ca = 40.08

**Calcii Carbonas** (*B.P., U.S.P. XI, P. Helv. V, P. Dan*)  
 $\text{CaCO}_3 = 100.08$ . *Syn* CALCII CARBONAS PRÆCIPITATUS, PRECIPITATED CALCIUM CARBONATE, PRECIPITATED CHALK, CRAIE PRÉPARÉE, GEFÄLLTES CALCIUM CARBONAT.

*Dose.*—15 to 60 grains (1 to 4 g.).

White insoluble powder. Much employed in diarrhoea and dysentery and as an ingredient in tooth powders

Diarrhoea of gastric origin is well treated by calcium carbonate and calcium phosphate equal parts, a teaspoonful thrice daily

The best antacid without any other inorganic salt in the gastric hyperacidity syndrome and in gastric and duodenal ulcer—*J. Amer med Ass*, 1/1927, 1558

**Creta** (*B.P., U.S.P. XI*). *Syn.* CRETA PRÆPARATA.

*Dose.*— $\frac{1}{4}$  to 1 drachm (1 to 4 g.)

A native calcium carbonate purified by elutriation. Consists of the tests of cretaceous foraminifera such as *Globigerina* and *Textularia*, together with minute rounded bodies (morpholites), and contains when dried not less than 97% of  $\text{CaCO}_3$ . Insoluble in water or alcohol.

**Blair's Tooth Powder.** Dissolve 3 of soap in about 4 of water, mix intimately with about 25 of precipitated chalk and dry at moderate heat. Dissolve catechu 1 in alcohol 5 and mix intimately with precipitated chalk 25. Mix equal parts of oil of wintergreen and oil of sassafras with a further 25 of precipitated chalk, using 6 drops of mixed oils for each 100 g. of powder. Mix the three portions and sift—*Pharm J.*, 1/1922, 263

**Creta cum Camphora** (*B.P.C.*). *Syn* CAMPHORATED CHALK  
 Camphor 10% in calcium carbonate.

**Mistura Cretæ** (*B.P.C.*). Chalk Mixture.

*Dose.*— $\frac{1}{2}$  to 1 ounce (15 to 30 ml.)

Contains 3% with sugar 6% and a little tragacanth, in cinnamon water. The powders are generally kept mixed in a dry condition, and cinnamon water added as required.

**Mistura Cretæ** (*U.S.P. XI*).

*Average dose.*— $\frac{1}{2}$  ounce (15 ml.).

Compound chalk powder 20, cinnamon water 40, in water to 100.

[P1] **Mist. Cret. Aromat. c. Opio** (*N.I.F.*).

Aromatic powder of chalk 20 gr., compound powder of tragacanth 5 gr., tincture of catechu 10 m, tincture of opium 5 m, chloroform water to  $\frac{1}{2}$  oz.

[P1] **Mistura Cretæ Composita** (*B.P.C.*).

*Dose.*—For adults, 1 ounce (30 ml.); for a 12 year old child,  $\frac{1}{2}$  ounce (15 ml.); for a 7 year old child, 2 drachms (8 ml.).

1 oz. contains 9 gr. of aromatic powder of chalk, 9 gr. of chalk,  $\frac{1}{2}$  dr. of tincture of catechu and 3 m. of tincture of opium.

Closely resembles the mixture formerly known as Board of Health Cholera Mixture

**Pulvis Cretæ Aromaticus (B.P.)**

*Dose*.—10 to 60 grains (0.6 to 4 g.).

Contains 25% of chalk, with cinnamon, nutmeg, clove, cardamom and sucrose.

**Pulvis Cretæ Compositus (U.S.P. XI).**

*Average dose*—30 grains (2 g.)

Prepared chalk 30, acacia 20, sucrose 50

**Sys Specific.** An Indian cure for sprue, dysentery and diarrhoea. It consists of "powders" containing principally calcium carbonate—one to be mixed with 12 ounces of water and laudanum to be added, if necessary.

**Trochisci Antacidi (B.P.C.)** contain calcium carbonate  $3\frac{1}{2}$  gr., heavy magnesium carbonate  $2\frac{1}{2}$  gr. and sodium chloride 1 gr.

**Unguentum Cretæ (B.P.C.)** 20% in spermaceti ointment

**Os Sepiæ (B.P.C.)** Cuttle Fish Bone. The internal shell of *Sepia officinalis* (Cephalopoda). Contains 80 to 85% of calcium carbonate, and is used as a mild abrasive in tooth powders.

**Sepia** is prepared from the fluid in the ink gland of the cuttle fish by drying, dissolving in alkali and reprecipitating with acid. Is used in homœopathy.

**Calcii Gluconas (B.P. Add, U.S.P. XI).**

$[\text{CH}_2\text{OH}(\text{CHOH})_4\text{COO}]_2\text{Ca} \cdot \text{H}_2\text{O} = 448.3$ .

*Dose*—30 to 60 grains (2 to 4 g.) *U.S.P. XI* average doses—oral, 75 gr., intravenous, 15 gr.

A white crystalline and granular powder soluble 1 in 30 of water, 1 in 5 of boiling water. Contains 8.9% of calcium. Gluconic acid,  $\text{C}_6\text{H}_6(\text{OH})_5\text{COOH}$ , is formed by oxidation of glucose, sucrose, dextrin or starch. It is a syrupy compound soluble in water.

Proprietary concentrated solutions of calcium gluconate are supersaturated solutions stabilised by patented methods.

**Uses.** Taken by the mouth, it is well absorbed. Intravenously it is better tolerated than calcium chloride. The acid-base factor is eliminated. Intramuscularly it is painless and non-irritant. It is at present the only calcium salt which can be given into the muscles in adequate dose. It is said to be almost specific in hay fever, and has influence on many respiratory diseases, relaxing bronchial spasm and decreasing secretion of mucosa of the respiratory tract. Also used in debility, malnutrition, neurasthenia, rheumatic cardiac manifestations and urticaria.

Maximum tolerated dose in dogs intravenously of calcium gluconate and calcium lactate 35 to 40 mg. of calcium ion per kilo, or 1.5 g. in 30 ml. water for an 8-kilo dog. Caused rise of blood pressure and fall in pulse rate (both more persistent with the gluconate), and digitalis-like effects. Over-dosage caused Cheyne-Stokes' respiration. Margin between effective and toxic doses not great. Intravascular clotting the greatest danger—*gives no warning and may cause sudden fatality*—A. L. Lieberman, *J. Pharmacol.*, Sept., 1930, 69.

The administration of calcium salts intravenously, following the administration of digitalis or one of its purified proprietary modifications, is a procedure of considerable hazard and may result in avoidable fatalities. Two deaths occurred following the intramuscular administration of digitalis and the intravenous injection of calcium gluconate. The manufacturers of calcium gluconate or chloride should preface their literature with a warning relative to the additive effect of calcium and digitalis when given simultaneously.—J. O. Bower and H. A. K. Mengle, *J. Amer. med. Ass.*, 1/1936, 1153.

**ECLAMPSIA**—Hyperguanidinæmia is associated with hypocalcæmia 7 g (total) of calcium gluconate intravenously, intramuscularly and subcutaneously, cured in 24 hours. Eclamptic syndrome yields to calcium medication—*Brit med. J. Epit.* 11/1930, 42

**MILK FEVER** cured by injecting calcium gluconate, also prophylactic.—*Lancet*, 11/1930, 411.

**ŒDEMA** of children suffering from nephrosis treated—*Brit med. J. Epit* 1/1931, 102.

**SERUM SICKNESS.** The following treatment was given in 15 cases as soon as a rash developed. 10 or 20 ml of 20% calcium gluconate intravenously, supplemented by 10 ml of 10% calcium gluconate intramuscularly, and the intramuscular injection repeated 12-hourly till rash or symptoms subsided, the solution for intravenous injection was warmed to body temperature and injected slowly (10 ml. in 2 or 3 minutes). As compared with 15 control cases (treated with adrenaline subcutaneously, ephedrine *per os*, calamine lotion locally, and sedatives), the rash in those treated with calcium lasted only 2.9 days against an average of 5.4 days, and subjective symptoms (itching, arthralgia, headache, cramps, nausea, etc.) 3.3 against 7.1 days.—T. J. Curphey and S. Solomon, *New Engl. J. Med.*, 1936, 214, 148

**TOXÆMIA OF PREGNANCY.** On the basis of a low calcium content, and accompanying deficiency of alkali, in this condition, good results have been obtained with a mixture of calcium sodium lactate 7½ gr, potassium citrate 40 gr, sodium bicarbonate 20 gr. In the pre-eclamptic state, give intravenously 10 ml. of calcium gluconate mixed with sterilised potassium citrate and sodium bicarbonate in a pint of boiled water—S. J. Cameron, *Lancet*, 11/1932, 731, see also W. C. Armstrong, *ibid*, 1328

**Calcium L-B** (*Allen & Hanburys, London*) Calcium lactobionate. Supplied in solution in ampoules, 2 g in 5 ml. For intramuscular or subcutaneous injection in calcium deficiency. Also combined with parathyroid in tablets and elixir

**Calcium Sandoz** (*Sandoz Products, London*) Preparations of calcium gluconate for oral, intramuscular or intravenous administration. Available as powder or as chocolate-flavoured or effervescent tablets, also in ampoules of 10% solution.

**Gluco-Calcium** (*Lilly, London*) Combination of calcium with glucose degradation products. Dose—3 to 5 ml intramuscularly and 5 to 20 ml intravenously. Tuberculosis, asthma, hay fever, etc

**Selvorol** (*Bayer Products, London*). Calcium salt of glucohexacetic acid containing 8.5% of Ca. Administered orally in doses of 30 gr. twice daily. Asthma, hay fever, urticaria and calcium deficiencies

**Calcium Lævulinate.** *Syn.* CALCIUM LÆVULATE

Contains 14.83% Ca as against 8.95% in the gluconate. Stable, very soluble and rapidly assimilable. 15% solution in 2 ml ampoules for intramuscular injection, 10% solution in 10 ml. ampoules for intravenous injection. Is non-irritant, and no sloughing occurs even if all is injected round the vein instead of into it.

Chronic tetany cured by 21 daily intramuscular injections of 5 ml. 3% solution.—T. Izod Bennett, *Lancet*, 11/1931, 403. See also G. Slot, *ibid*, 556.

**Tetanol** (*British Colloids, London*). A solution of calcium levulinate.

*Dose.*—Intravenously, 5, 10, or 20 ml. 13% solution, intramuscularly, 2 ml 20% solution.

**Calcii Hydroxidum** (*B.P., U.S.P. XI*). *Syn.* CALCIUM HYDRAS.  $\text{Ca(OH)}_2 = 74.10$ . Should be recently made by action of water on calcium oxide. Is more soluble in cold water than in hot.

**Linimentum Calcii Hydroxidi** (*B.P.C.*).

Solution of calcium hydroxide 1, olive oil 1.

**Linimentum Calcii Hydroxidi cum Oleo Lini** (*B.P.C.*).

*Syn.* CARRON OIL.

Solution of calcium hydroxide 1, linseed oil 1. Eucalyptus oil 1 to 2% is sometimes added as antiseptic.

Burns are treated with it, but it is thought to be out of date. Tannic acid is now advised, *q.v.*

**Liquor Calcii Hydroxidi (B.P.)** *Syn.* LIQUOR CALCIS, LIME WATER

*Dose.*—1 to 4 ounces (30 to 120 ml.).

Contains not less than 0.15% *w/v* of  $\text{Ca}(\text{OH})_2$ . It is given with milk to infants to prevent formation of large clots.

Warts (*verruca plana*) on the back of the hand are stated to have been cured in a week by  $\frac{1}{2}$  pint a day.

**Liquor Calcii Hydroxidi Saccharatus (B.P.C.)** *Syn.* LIQUOR CALCIS SACCHARATUS

*Dose* —  $\frac{1}{4}$  to 1 drachm (1 to 4 ml.)

Contains the equivalent of 2.4% *w/v* of  $\text{Ca}(\text{OH})_2$  with sucrose and water

**Liquor Calcii Hydroxidi (U.S.P. XI)**

*Average dose* —  $\frac{1}{4}$  ounce (15 ml.)

Same as *B.P.*, but made with 3 g of calcium hydroxide for each litre of solution

**Calcii Oxidum.** *Syn.* QUICKLIME

White or greyish-white masses. Used as a caustic, *e.g.*, in *Pasta Londinensis (q.v.)* **Soda-lime** is prepared by shaking quicklime with sodium hydroxide solution and heating to redness.

**Calcii Saccharas.** *Syn.* CALCIUM MONOSACCHARATE.

$\text{C}_{12}\text{H}_{22}\text{O}_{11}\text{CaO} = 398.2$

*Dose* — 8 to 30 grains (0.5 to 2 g.)

In colourless tufts, soluble in water. An antacid for dyspepsia, specially for children, also as an antidote to carbolic acid poisoning in 10 times above doses

**Calcii Sulphas.**  $\text{CaSO}_4 \cdot 2\text{H}_2\text{O} = 172.2$

*Dose.*—20 to 30 grains daily (1.2 to 2 g.)

A heavy white powder soluble in water 1 in 390

For phosphaturia is considered a specific; it may be given with an equal weight of heavy magnesium carbonate

**Calcii Sulphas Exsiccatus (B.P.C., P. Helv. V).** *Syn.* PLASTER OF PARIS.  $\text{CaSO}_4 \cdot \frac{1}{2}\text{H}_2\text{O} = 145.1$  A white, hygroscopic, odourless powder. Two pounds require about 1 pint of water; this sets rapidly and firmly.

Moistening with 5% dextrin solution makes a strong dressing but sets slowly. Sodium chloride 1% added hastens setting but 2% retards.

**Ligamentum Calcii Sulphatis (B.P.C.)** Plaster of Paris bandages consist of bleached cotton cloth impregnated with the plaster and suitable adhesives.

**Calx Sulphurata (B.P.C.).** *Syn.* CALCII SULPHIDUM CRUDUM; CANTON'S PHOSPHORUS. Contains not less than 50% of  $\text{CaS} = 72.14$ .

*Dose.*— $\frac{1}{4}$  to 1 grain (0.016 to 0.06 g.) in pill.

Is prepared by reducing calcium sulphate with charcoal. A greyish powder with odour of hydrogen sulphide. Sparingly *soluble* in water with decomposition. It thus represents the properties of Harrogate, Barèges, Gilsland, and similar springs. Largely used for boils, carbuncles, acne, scrofulous sores, and especially in glands of the neck. It rarely purges even in 2 grain doses thrice daily. Some give small doses *every hour*.

In strumous ophthalmia, as well as in periostitis and alveolar abscesses, has been found of service. Also in follicular tonsillitis. For boils give 1 grain *t.d.*, increased to 8 grains *p.d.*

**ACNE** Good results claimed with doses of not less than 2 grains 3 times a day—A. Whitfield, *Brit J Dermat*, 1934, 257.

**PUERPERAL SEPSIS** Calcium sulphide in doses varying from 1½ to 12 grains per 24 hours reduced the death-rate from sepsis in the County Maternity Hospital, Bellshill, Lanark, from 5.3 per 1000 in cases confined within the institution from 1927 to 1933 inclusive (5,421 cases) to 0.7 per 1000 for 1933 to 1935 inclusive (2,518 cases). Used either as a prophylactic previous to confinement or even during the puerperium, it not only prevents the incidence of puerperal infection, but also does much to curtail the mortality.—H. J. Thomson, *Brit med J.*, 11/1935, 1070

**Liquor Calcis Sulphuratæ (B.P.C.).** *Syn.* LOTIO CALCIS SULPHURATÆ, VLEMINCKX'S SOLUTION, CALCIUM SULFURATUM SOLUTUM (P. *Helv* V).

Prepared by boiling sulphur with calcium hydroxide and water, and contains polysulphides of calcium equivalent to 4 to 5% *w/v* of sulphur.

Valuable in Dhobie's itch, at first used diluted 3 or 4 times

For eczematous itching, baths of the solution, 1 tablespoonful to every 7 gallons of water, have been used

In scabies found too irritating for use. Not equal to a weak sulphur ointment in curative effect. Freshly precipitated sulphur has been used by washing the patient first with a dilute sodium thiosulphate solution, and then with dilute hydrochloric acid. Subsequently to allay irritation, sulphur ointment.

**Tabellæ Calcis Sulphuratæ (B.P.C.).** *Syn.* TABELLÆ CALCII SULPHIDI. Contain ½ gr. (0.03 g.).

**Colloidal Calcium.** Preparations of colloidal calcium usually contain the metal in the form of a compound. The usual strength is 1 in 2000.

*Dose.*—8 to 15 minims (0.5 to 1 ml.) hypodermically, ½ to 1 drachm (2 to 4 ml.) orally. Is used for the general purposes of calcium therapy.

Empyema, ischio-rectal abscesses and hay fever have been well treated with colloidal calcium—E. E. Prest, *Brit med. J.*, 11/1927, 958.

## CAMPHORA

*B.P., U.S.P. XI, P.G. VI, F.E. VIII, P. Dan., P. Helv. V.*

$C_{10}H_{16}O = 152.1$ .

*Dose.*—2 to 5 grains (0.12 to 0.3 g.); 1 to 3 grains (0.06 to 0.2 g.) by subcutaneous injection.

Camphor is a white crystalline substance obtained from *Cinnamomum Camphora* (Lauraceæ) in Formosa and Japan, or obtained synthetically from the pinene of oil of turpentine. M p 174° to 177°; b.p. 204°.

Camphor is sold in bells, and in  $\frac{1}{4}$ ,  $\frac{1}{2}$ , 1 and 4 ounce cubes, also as **Flowers of Camphor**. The latter is a convenient form for dissolving

**Soluble** 1 in 700 of water, 1 in  $1\frac{1}{2}$  of alcohol 90% (more soluble in dehydrated alcohol), 12 in 7 of ether, about 4 in 1 of chloroform, 2 in 1 of glacial acetic acid, and 1 in 3 of olive oil. Also soluble in other fixed and volatile oils

It is rendered more soluble in water by the presence of carbon dioxide, acid carbonate and carbonate of magnesium, sugar and myrrh, and less soluble by potassium bromide, Liquor Potassæ, magnesium sulphate, alkaline carbonates and many other salts.

Camphor, when mixed in certain proportions with many crystalline substances, causes mutual liquefaction of the two—*e.g.*, camphor 4, phenol 12, and water 1, camphor 1 and chloral hydrate 1, camphor 2 and menthol 3; camphor 1 and thymol 1, camphor 2 and  $\beta$ -naphthol 1; camphor 2 and salol 3, camphor and butyl-chloral hydrate liquefy when heated, but solidify on cooling, so will camphor 84 and salicylic acid 65 Camphor is powdered by rubbing with a few drops of alcohol

**Antidotes.** Empty stomach by emetic or stomach tube Give purgative dose of magnesium sulphate in plenty of water. Keep patient warm, and give inhalations of ether or dilute ammonia Stimulants, *e.g.*, digitalin  $\frac{1}{2}$  gr, strychnine  $\frac{1}{2}$  gr, caffeine sodium benzoate 2 gr., hypodermically

**Caution.** It is dangerous to place camphor or menthol, *e.g.*, a 20% ointment, into the nostrils of an infant A small quantity applied in this way may cause immediate collapse with signs of a severe syncopal attack

**Poisoning** from 75 grains of camphor as camphorated oil Recovery Stomach washed out and several ounces concentrated magnesium sulphate solution left in —J Cottrell, *Brit. med J*, 1/1931, 96

**Uses.** Sedative, anti-spasmodic, carminative, expectorant, diaphoretic, anaphrodisiac, antiseptic, given internally to abort colds in the head, to relieve hiccough, for whooping cough, diarrhœa, chordee and lumbago For arteriosclerosis and for old patients with heart trouble continued use of camphor internally is of value Is injected as a stimulant for patients *in extremis*, and valuable, in doses of  $1\frac{1}{2}$  gr per day in oil, throughout entire course of various cardiac and vascular diseases

It is no exaggeration to say that experienced pharmacologists would find great difficulty in supporting the claims of clinicians that camphor in oil is a powerful stimulant of respiration and circulation It is difficult to assess the value of its use in collapsed and moribund patients —E. C Dodds, *Proc R. Soc. Med.*, 1936, 29, 656

SCIATICA and NEURITIS well treated —Jensen, *Brit med J Epit*, 1/1920, 17

**ENGORGEMENT OF BREASTS** Intramuscular injections of  $1\frac{1}{2}$  grains of value Has inhibiting action on milk secretion. Give two injections the first day and one for each of next three days —W Philphot, *J Amer med Ass*, 11/1929, 65

**Camphor Ball.** Spermaceti 4, white wax 12, almond oil 5; melt in a water-bath and add flowers of camphor 4. Dissolve, and when nearly cold pour into moulds. Useful for chapped skin.

**Aqua Camphoræ (B.P.).** *Syn.* CAMPHOR JULEP, MIST. CAMPHORÆ. 1 in 1000. 60 minims of spirit of camphor added to 12 oz of water gives a solution of approximately the same strength. Camphor water (*U.S.P. XI*) is a saturated solution.

**Aqua Sedativa.** *Syn.* EAU SÉDATIVE, LOTION AMMONIACALE CAMPHRÉE (*Fr. Cx.*). Spirit of camphor (10%) 10, sodium chloride 60, solution of ammonia 60, distilled water 1000, all by weight.

As a compress for migraine and rheumatism, and to contusions

**Teinture de Camphoræ Faible** (*Fr. Cx.*) is 1 in 40 of alcohol 60%.

**Aqua Camphoræ Concentrata (B.P.C.).**

*Dose.*—5 to 15 minims (0.3 to 1 ml). 1 part equals 40 parts of camphor water

**Elixir Camphoræ.** *Dose.*— $\frac{1}{2}$  to 1 drachm (2 to 4 ml)

Spirit of camphor 10, syrup 5, distilled water 1. Contains 1 in 16. It mixes and diffuses well in water.

**Injectio Camphoræ (B.P.C.).** *Syn.* HUILE CAMPHRÉE STÉRILISÉE POUR INJECTION HYPODERMIQUE (*Fr. Cx. Supp.* 1926)

*Dose.*—8 to 30 minims (0.5 to 2 ml). *Fr. Cx. Supp.* 1926 gives max. in 24 hours 100 ml. (*caution*).

10% w/v in olive oil

In pneumonia 25 minims has been given as a general rule to start with, but much larger doses have been employed—even 12 ml. of a 20% solution.

**Injectio Camphoræ Ætherea (B.P.C.).** *Syn.* CURSCHMANN'S SOLUTION

*Dose.*—4 to 15 minims (0.25 to 1 ml).

Camphor 20% w/v and ether 30 v/v in olive oil.

**Caution.** Various amounts (30 to 300 ml) of 1 to 10% solution have been injected. A case recorded of acute poisoning from 170 ml of 10% solution after an operation. 1% may be safe and not more than 300 ml of this solution.

Urticaria following the use of injections—*Per J. Amer. med. Ass.*, 11/1925, 476

**Injectabile Camphoræ Æthereus (P. Helv. V).** *Syn.* ÆTHER CAMPHORATUS. Camphor 1 g, anæsthetic ether to 10 ml

[P1] **Linctus Camphoræ Compositus (B.P.C.)**

*Dose.*— $\frac{1}{2}$  to 2 drachms (2 to 8 ml)

Camphorated tincture of opium, 1 in 4, in a wild cherry, squill and senega menstruum.

**Linimentum Camphoræ (B.P.).** *Syn.* CAMPHORATED OIL; OLEUM CAMPHORATUM (*P. Dan.*)

Camphor 20% w/w in olive oil.

**Linimentum Camphoræ (U.S.P. XI).** 20% w/w of camphor in cottonseed oil.

Cottonseed oil unsatisfactory for camphor liniment. Likely to congeal to consistence of cheese.—*J. J. Blackie, Pharm. J.*, 1/1931, 17

**Oleum Camphoratum, Huile Camphrée** (*Fr. Cx.*) 1 to 9 of olive oil.

[P2] **Linimentum Camphoræ Ammoniatum (B.P.).** *Syn.* LINIMENTUM CAMPHORÆ COMPOSITUM.

Camphor 12.5% *w/v*, strong solution of ammonia 25% *v/v* and oil of lavender in alcohol or methylated spirit

**Linimentum Camphoræ et Saponis (U.S.P. XI)**

Camphor 4.5% and hard soap 6%, with oil of rosemary, in alcohol and water

**[P1] Pigmentum Camphoræ Chloral et Menthol.**

Camphor, chloral hydrate and menthol, equal parts. Useful in acute fibrositis, rubbed in gently with the fingers

**Pilula Camphoræ.**

To form camphor into pills use  $\frac{1}{2}$  its weight of powdered curd soap and a few drops of alcohol, or a little lard in a warm mortar

**Spiritus Camphoræ (B.P.).**

*Dose* —5 to 30 minims (0.3 to 2 ml).

Contains 10% *w/v* of camphor in alcohol 90%.

**Spiritus Camphoræ (U.S.P. XI)**

*Average dose* —15 minims (1 ml)

Camphor 9.5 to 10.5% *w/v* in alcohol

**Æther Spirituosus Camphoratus (P. Dan.)** *Syn.* KAMFERDRAABER  
10% *w/v* in spirit of ether 25% *w/w*

**Spiritus Camphoræ Fortior** *Syn.* RUBINI'S SOLUTION

Flowers of camphor 1, absolute alcohol (by weight) 1 *Dose* for diarrhoea.—2 to 5 drops on sugar every 5, 10 or 15 minutes, according to the severity of the symptoms

**[P1] Syrupus Camphoræ Compositus (B.P.C.).**

*Dose* — $\frac{1}{2}$  to 1 drachm (2 to 4 ml.)

Contains  $\frac{1}{4}$  gr of camphor and 1 m of tincture of opium with oil of anise, benzoic acid, glacial acetic acid, vinegar of ipecacuanha and vinegar of squill in a syrup basis to 1 dr.

**Tablets of Camphor and Quinine.** Camphor  $\frac{1}{2}$  gr, with quinine acid sulphate 1 gr To check catarrh and as a tonic

**Unguentum Camphoræ (B.P.C.)** 10% in white soft paraffin.

**Unguentum Camphoræ Durum (B.P.C.)** *Syn.* CAMPHOR ICE. 6% in hard and soft paraffins.

**Acidum Camphoricum (B.P.C., P. Ned. V, P. Helv. V, P. Jap. IV, F.E. VIII)**  $C_8H_{14}(COOH)_2 = 200$  1.

*Dose*.—8 to 30 grains (0.5 to 2 g) in cachets or suspended with tragacanth in a mixture

Formed on oxidation of camphor with nitric acid. Odourless crystals, dextrorotatory, m.p. 185° to 187°.

**Soluble** about 1 in 160 of water, about 1 in 1 $\frac{1}{2}$  of alcohol 90% and 1 in 10 of fatty oils; also soluble in ether, but only slightly in chloroform.

**Uses.** With success in night sweats of phthisis, also in cystitis by intravesical injections of 2% aqueous solution with 11% alcohol, and as an intestinal disinfectant. Further in solution as a local astringent for nose and throat, also for diarrhoea. In skin affections saturated solution in dilute alcohol locally useful.

**Camphoræ Monobromidum (B.P.C., P. Helv. V, P. Ital. V, P. Jap., F.E. VIII, P. Belg. IV, and P. Ned. V).** *Syn.* CAMPHORA MONOBROMATA, 3-BROMOCAMPHOR.  $C_{10}H_{15}OBr = 231.0$ .



**Dose.**—2 to 8 grains (0·12 to 0·5 g.), in pills with  $\frac{1}{3}$  of its weight of curd soap and proof spirit *q s.*, or dissolved in oil and emulsified.

In colourless prisms with persistent camphoraceous taste  
**Soluble** 1 in 12 of alcohol 90%, 1 in 2 of ether, 10 in 7 of chloroform, 1 in 8 of olive oil, sparingly soluble in glycerin, soluble in sulphuric acid with formation of nearly colourless solution. It is used as a hypnotic, and is of value in epileptic vertigo, cases of petit mal, chorea, hysteria, delirium tremens, whooping cough and asthma, and for erections in gonorrhœa.

**Elixir Camphoræ Monobromatæ**

Camphor monobromide 1, spirit of cinnamon (1 in 10) 10, dissolve and add red elixir 60, syrup *q s.* to 100 **Dose**— $\frac{1}{2}$  ounce

Enuresis is treated with this combined with belladonna, where potassium bromide is unsuitable

**Camphora Salicylata.** **Dose**—1 to 5 grains (0·06 to 0·3 g.), in pill with suet or lard.

Camphor 56, salicylic acid 44, combined Soluble about 1 in 20 in oils and alcohol As ointment in skin affections

**Trochisci Camphoræ Salicylatæ Compositi.** Camphor salicylate 2 grains, sodium sulphate 4 grains One thrice daily an hour before food To ward off a cold

[P1] **Calmitol** (*Napp, London*) "Ether-alcoholic solution of camphor aldehyde slightly iodised, with the addition of menthol and a trace of hyoscine oleate" Lotion or ointment for use in all forms of skin irritation

**Camphemyl** (*Ciba, London*) 10% solution of camphor in a mixture of methyl urethane, monoethyl urea and distilled water An improvement on oily solutions

**Cardatone** (*Evans, Sons, Lescher & Webb, Liverpool*) An aqueous solution containing 15% of sodium campho-sulphonate. A non-toxic analeptic for use as a cardiac and respiratory stimulant

**Dose**—1 or 2 ml subcutaneously, intramuscularly or intravenously, or 1·5 to 6 ml of a special solution *per os* In cases of poisoning by carbon monoxide, gas, narcotics, etc., as much as 5 to 15 ml may be given intravenously, in collapse during narcosis, 2 to 6 ml. may be injected intravenously followed by up to 5 ml intramuscularly.

The difficulty of the insolubility of camphor has been overcome by the use of the easily soluble sodium salt of camphorsulphonic acid (sodium camphor-sulphonate), and it has been recommended that it should be used in a 15% solution The toxicity of this compound is very slight, and pharmacological experiments have shown it to possess all the activity of camphor with the added advantage of solubility Thus the slight, but definite, action of camphor on respiration and the cardiovascular system is rendered surer through even distribution and absorption Its use has been recommended in cases in which stimulation of a patient who is to receive a transfusion is required.—E. C. Dodds, *Proc R Soc Med*, 1936, 29, 658.

**Cardiazol** (*Knoll, Ludwigshafen, Pharmaceutical Products, London*). **Syn.** METRAZOL, PENTAMETHYLENETETRAZOL ( $\text{CH}_2)_4\text{N}_4$ .

A rapidly-acting cardiovascular excitant for oral, subcutaneous, intramuscular, intravenous or rectal administration Occurs as a white powder, m.p. 56° to 58°, readily soluble in water. Solutions may be sterilised by heat Available in powder, in tablets containing 1½ gr., in 1 or 3 ml ampoules and in 10% solution

**Dose.**—1½ gr. (1 tablet disintegrated in water, or 1 ml of the liquid) 3 or 4 times daily, or more frequently if necessary. One ampoule (1 ml) may be given subcutaneously every ½ to 1 hour. Suppositories may be made with 0.1 to 0.2 g. in 2 g of oil of theobroma.

[D-P1-81] **Cardiazol-Dicodid Drops.** 20 drops correspond to about 1½ gr of cardiazol and ½ gr of dicodid hydrochloride. **Dose**—Start with small doses to establish tolerance; infants and young children 2 to 5 drops 2 to 3 times daily, older children 5 to 10 drops 3 times daily, adults 10 to 20 drops. Cough, whooping cough, asthmatic and stenocardiac conditions

[P1] **Cardiazol-Ephedrine**, a combination of the above with ephedrine hydrochloride, for bronchial asthma, circulatory collapse and collapse during narcosis. Each tablet or each ml of solution contains ½ gr of ephedrine hydrochloride

**Cardiazol-Quinine.** Tablets contain ½ gr of Cardiazol and 1½ gr. quinine hydrochloride (*dose*—2 to 3 daily), ampoules of 1 ml contain 1½ gr of Cardiazol and 4 gr of quinine lactate in aqueous solution (*dose*—2 to 3 daily intramuscularly), suppositories contain 1½ gr of Cardiazol and 4 gr of quinine valerianate. Catarrhal symptoms and infectious diseases, disorders associated with high temperatures and circulatory disturbances, disordered cardiac conductivity

Observations on 96 patients who had been anaesthetised with Evipan, ether, or Avertin, and who had been awakened by an intravenous injection of 5 ml of Cardiazol. In most cases the effect was very prompt, even during the injection, which was given very slowly, the respiration became deeper and in some cases more frequent, the pulse meanwhile becoming stronger and more regular. The improvement thus effected in the action of the heart was so marked in some cases that, although a saline infusion had previously seemed necessary, it now became superfluous. With the exception of four cases (abdominal operations) there was an appreciable shortening of the post-operative unconsciousness, and thus the risk of aspiration accidents was reduced.—Pieniezny, *Dtsch med Wschr*, 1935, 1641

**Coramine (Ciba, London)** Pyridine-β-carbonic acid diethylamide,  $C_5H_4N \cdot CO \cdot N(C_2H_5)_2$ , a yellowish liquid miscible with water. Supplied as a 25% solution flavoured for oral use, and in 1 ml. ampoules. For shock, collapse, circulatory failure, asphyxia of the newborn, heart asthenia and generally as a substitute for camphor injections

**Dose**—Orally, 15 to 30 minims (1 to 2 ml) with a little water. In chronic hyperpiesis 25 m. twice daily in water. Hypodermically, intramuscularly, intravenously or intracardially, 1 or 2 ampoules. Repeat in a few hours if necessary.

The intravenous or intramuscular administration of Coramine can decrease the duration of postpartum narcosis due to barbituric acid drugs—A. A. Levi and C. M. Krinsky, *New Engl J Med*, 1936, 214, 364

**Calcio-Coramine (Ciba, London)** Double salt of pyridine-β-carbonic acid diethylamide and calcium thiocyanate. Tablets contain 6 gr. **Dose.**—1 or 2 tablets 3 times a day after meals. Cardiac and respiratory stimulant and expectorant in bronchitis, catarrh, broncho-pneumonia, emphysema, etc.

**Icoral (Bayer Products, London)** A 5% solution of a mixture of the hydrochlorides of *m*-oxyethyldiethylaminoethylaminobenzol and *m*-oxy-*n*-phenylpropanolamine, mixed in the ratio of 4 parts of the former to 1 of the latter. A respiratory and cardiac stimulant used with success in barbituric acid poisoning, carbon monoxide poisoning, morphine poisoning and in a case of quinsy with suffocation. Of no value in severe infections with collapse of purely vasomotor type. Injected intravenously with care (except in cases of severely damaged myocardium) in dose of 0.3 ml. repeated in 20 minutes.—H. Frank, *Dtsch med Wschr*, 1/1933, 764

**Solucamphre (Delalande, Paris, Roberts & Co, London)** Water-soluble camphor. 14% solution of *d*-camphor sulphonate of diethylenediamine. **Dose.**—1 to 3 injections of 5 ml. daily subcutaneously or intramuscularly, or an injection of 2 to 5 ml intravenously in urgent cases. Also as drops, 50 to 100 dilv. To replace camphor in oil as a cardiac and respiratory stimulant

**Oleum Camphoræ Rectificatum (B.P.C.).** *Syn.* WHITE OIL OF CAMPHOR, OLEUM CAMPHORÆ ESSENTIALE.

Consists of the lighter fractions of the oil obtained in the manufacture of natural camphor. It varies in composition according to the extent to which camphor and saffrole are removed. The heavier fractions of the crude oil are used as a source of saffrole and are known as "brown oil of camphor." The rectified oil contains not less than 35% of cineole. Is used as a mild counter-irritant in rheumatism, and as a parasiticide.

**Moschus (B.P.C.).** Musk.

*Dose.*—5 to 10 grains (0.3 to 0.6 g.).

The sac containing the dried secretion from the preputial follicles of the musk deer, *Moschus moschiferus* (Ungulata).

**Grain musk** (*Moschus in grano*) is the dried granular secretion. A useful nerve stimulant in cases of exhaustion in fevers and blood poisoning. Of value both for nervous excitement or nervous collapse. Is effective in obstinate hiccough and infantile convulsions. The odour of musk is due to muskone,  $C_{15}H_{28}O$  or  $C_{16}H_{30}O$ . The butyl derivatives of many aromatic hydrocarbons are sold as **artificial musk**, e.g., MUSK AMBRETE is dinitro-*tert*-butyl-*m*-cresylmethylether,  $C_6H(C_4H_9)(CH_3)(OCH_3)(NO_2)_2$ .

Musk, civet and castor. Notes on the chemistry of these aromatic animal secretions—*Chem and Drugg*, 1/1930, 228

**Mistura Moschi.** Musk 5 gr., acacia 5 gr., syrup of orange 1 dr., rose water to 1 oz

**Tinctura Moschi.** *Dose*— $\frac{1}{2}$  to 1 drachm (2 to 4 ml) 1 in 20 of alcohol 50%. A tincture of artificial musk has been used in whooping cough. In cardiac failure of acute pneumonia it has been given alone in cachets or with camphor in pills

**Sassafras (B.P.C.)** is the dried inner bark of the root of *S. varunifolium* (Lauracæ). Is carminative by virtue of its oil content

**Sassafras Medulla** is the pith from the stem of *S. officinale*. Forms with water a demulcent mucilage which has been used in eye lotions

**Sassafras Radix** is the root of *S. officinale*. Contains about 2% of volatile oil.

**Sassafras Cortex** is described in *P. Helv V*

**Safrolum (B.P.C.).** *Syn.* SAFROL OF SAFROLE, ALLYL CATECHOL METHYLENE ETHER.  $C_6H_5 \cdot C_3H_5 \cdot O \cdot OCH_2 = 162.1$

Is the chief constituent of oil of sassafras but is obtained from essential oil of camphor. Occurs as a colourless or yellowish oil with odour of sassafras. Is used for lice and nits in pediculosis. In treating ringworm, the hair is cut close to identify the patches, and the oil applied twice a day by a brush, treatment being continuous for a few weeks if necessary. Non-irritating, pleasant to use, prevents spread of infection and destroys the fungus. Saffrole is used also as a perfume for cheap soap, in the manufacture of heliotropin, and is occasionally added to anodyne liniments for rheumatism.

**Oleum Sassafras (B.P.C., U.S.P. XI).**

*Dose.*—1 to 5 minims (0.06 to 0.3 ml.). *U.S.P. XI* average dose 1½ minims.

A pale yellow or reddish oil containing about 80% of safrole. Is used to destroy pediculi, being applied to the hair with a stiff brush.

As an insecticide for dogs and cats safrol, or oil of sassafras, may be extremely toxic in some cases.—*Pharm. J.*, 11/1925, 576.

**CANNABIS***B.P.C.*

*Syn* CANNABIS INDICA (*U.S.P. XI*, *F.E. VIII*, *P. Belg. IV*, *P. Helv. V*), MARIHUANA

[D] "Indian hemp and resins obtained from Indian hemp and all preparations (except extract and tincture of Indian hemp) of which such resins form the base" (See p. 1033)

"Any extract or tincture of Indian hemp."

[P1] "Cannabis (the dried flowering or fruiting tops of *Cannabis sativa* Linn), the resin of cannabis; extracts of cannabis, tinctures of cannabis; cannabin tannate"

[81] "Cannabis, the resin of cannabis; extracts of cannabis; tinctures of cannabis; cannabin tannate."

Rule 10 of the Poisons Rules, 1935, exempts from the application of the Pharmacy and Poisons Act, 1933, and of the Rules made under that Act all corn paints in which the only poison is a poison included in the Poisons List under the heading of "Cannabis"

The dried flowering or fruiting tops of the pistillate plant of *Cannabis sativa* (Urticacæ). The *B.P.* '14 required the drug to be obtained from plants grown in India, but this requirement is not included in the *B.P.C.*, since African, American and German varieties are also pharmacologically active.

The masses obtained in European commerce are called Guaza. Ganja differs slightly and is more active Bhang or Hashish consists of the leaves, small stalks and fruits.

The therapeutic value of the drug is contained in the resin (cannabinone) which contains cannabinol,  $C_{21}H_{36}O_2$ . The latter becomes oxidised on exposure to the air and less active, but even long storage of whole cannabis does not destroy its activity. It is a powerful drug.

**Antidotes.** Empty stomach by emetic or stomach tube. Stimulants such as strong black coffee frequently. Strychnine, ½ gr., hypodermically. Keep patient warm. Artificial respiration may be necessary.

A case of cannabis indica intoxication from the smoking of cigarettes made from the dried leaves and tops of plants grown in England—E. T. Baker-Bates, *Lancet*, 1/1935, 811 See also W. A. J. Fleming, *ibid.*, 1301

According to authorities, in certain parts of the U.S.A. one out of every four persons is a marihuana smoker. Its use was first observed in seaports, but rather sporadically, then more regularly in the states adjacent to Mexico, and in the past eight years in the large cities all over the U.S.A. In California, and other states of the south-west, and in the larger metropolitan centres of the east, it has

already become a social and criminological problem. Addiction among marihuana users is unlike addiction among the users of morphine or heroin. With these latter the victim must have the drug to feel normal, but with marihuana the addict wants to recapture the pleasurable euphoric state into which the drug lifts him. It is more of a psychological condition—there is no marked physiological disturbance on withdrawal of the drug. After long usage, however, a dull state supervenes in which the victim is for all practical purposes an addict, and in which ethical and intellectual deterioration and apathy are the outstanding factors.—W. Bromberg, *Med Rec*, 11/1935, 309.

**Uses.** For chordee and asthma, also as an aphrodisiac, and is successful in migraine. Is a narcotic and anodyne, but may give peculiar dreams and even delirium.

It is useful in dysmenorrhœa, especially with gelsemium, and with nux vomica in incipient delirium tremens, nausea, and paroxysmal colic, supraorbital neuralgia, cough of phthisis and for whooping cough. It is of great use combined with chloral in chorea in mental worry and restlessness. Should be given in small and frequent doses. It is the remedy for menorrhagia.

In gonorrhœa (acute anterior urethritis) cannabis internally with hyoscyamus is useful before patient is in condition for injections.

HEADACHE DUE TO HIGH BLOOD PRESSURE well treated, especially where chronic interstitial nephritis is a contraindication to blue pill—A Feiling, *Brit med. J*, 11/1930, 907.

[D P1 81] **Extractum Cannabis (B P C).** *Syn* EXTRACT DE CHANVRE INDIEN (*Fr. Cx.* 1926 *Supp.*).

*Dose.*— $\frac{1}{4}$  to 1 grain (0.016 to 0.06 g.), in pill with lycopodium. A soft alcoholic extract.

[D P1 81] **Extractum Cannabis (U S P. XI).** *Average dose*— $\frac{1}{4}$  grain (0.015 g.). A soft or pilular extract.

[P1 81] **Mistura Cannabis Indicæ (C.H.W.)**

Tincture of cannabis 10 m., spirit of nitrous ether 30 m., solution of ammonium acetate 1 dr., mucilage q s., camphor water to 1 oz.

[P1 81] **Cannabinæ Tannas.**

*Dose*—4 to 8 grains (0.25 to 0.5 g.) taken an hour before bedtime in a pill or in sal volatile and water.

A brownish powder, soluble in alkaline water and alcohol, said to be a useful hypnotic and is specially valuable in nervous sleeplessness and in acute mania, also for dysmenorrhœa and menorrhagia.

Cannabin tannate not a "dangerous drug"—*l'harm J*, 11/1929, 462

**Cannabinone** has been used as a hypnotic in doses of  $\frac{1}{4}$  to 1 grain (0.016 to 0.06 g.).

[D P1 81] **Tinctura Cannabis (B.P.C.).**

*Dose.*—5 to 15 minims (0.3 to 1 ml.) 1 of extract in alcohol 90% to 20. When dispensed in mixtures, mucilage must be added to suspend the resin.

[P1 81] **Cannabis Sativa (P. Helv. V)** Russian hemp-seed, oil-free, has been used in form of decoction, strength 100 g. in 1 litre, heated gently and evaporated (without boiling) to 250 ml. 35 to 50 ml. of the resulting liquor is given to children in food.

[P1 81] **Emulalo Seminum Cannabis.** 10% in water. Used as a potion against gonorrhœa, two glasses daily. Has slight sedative properties.

[D P1-81] *Fluidextractum Cannabis* (U.S.P. XI).

Average dose.—1½ minims (0.1 ml.). 1 ml. represents 1 g. of the herb.

**Apocynum** (B.P.C.). *Syn.* AMERICAN INDIAN HEMP ROOT, CANADIAN HEMP.

*Dose.*—1 to 5 grains (0.06 to 0.3 g.). U.S.P. VIII average dose 15 grains. The rhizome and roots of *Apocynum cannabinum* and other species of *Apocynum* (Apocynaceæ). Stated to be a rapid and efficient cardiac stimulant, also an active non-cumulative diuretic, occupying a place between digitalis and caffeine.

A powerful emetic, diaphoretic, cathartic and anthelmintic, and diuretic, employed in cardiac dropsy and Bright's disease. The active principle is the glycoside cymarín

Apocynum rhizome varies enormously. It had a great reputation among the aborigines and early settlers for dropsy. There was confusion and substitution. Good apocynum is many times more active than digitalis as a heart stimulant.—H. H. Rusby, *Pharm. J.*, ii/1929, 312.

**Decoctum Apocyni.** *Dose.*—½ to 1 ounce. 1 in 60.

**Tinctura Apocyni** (B.P.C.). *Dose.*—5 to 10 minims (0.3 to 0.6 ml.); up to 1 fl. drachm (4 ml.) is sometimes given. 1 in 10 of alcohol 60%. Resembles tincture of digitalis in action but is more irritant. Is used as a diuretic in cardiac dropsy. Large doses may cause gastric ulcerations.

Uremia is warded off by the profuse diuresis it produces and it is of use in removing pleuritic effusion.

**Asclepias incarnata.** *Syn.* WHITE INDIAN HEMP RHIZOME. Is a speedy, potent and reliable diuretic. Tincture, 1 in 10. *Dose.*—5 to 40 minims.

**Asclepias tuberosa.** *Syn.* PLEURISY ROOT. Is expectorant and diuretic. Tincture, 1 in 10. *Dose.*—5 to 40 minims.

## CANTHARIS

B.P.C., U.S.P. XI, P. Dan., P. Helv. V.

*Syn.* LYTTE, SPANISH OR BLISTERING FLY.

[P1] "Cantharidin; cantharidates."

[81] "Cantharidin except substances containing less than 0.01 per cent. of cantharidin."

"Cantharidates except substances containing less than the equivalent of 0.01 per cent. of cantharidin."

By Rule 10 of the Poisons Rules, 1935, machine-spread plasters are exempt from the provisions applying solely to substances in the First Schedule to the Rules.

*Dose.*— $\frac{1}{16}$  to  $\frac{1}{8}$  grain (0.004 to 0.03 g.) in pill. Better given as tincture. *Fr. Cx.* max. single dose  $\frac{1}{8}$  grain; max. in 24 hours, 2 grains.

The dried beetle *Cantharis vesicatoria*, found in Southern Europe. It contains about 0.4 to 0.8% of cantharidin. *P. Jap. IV* has *Epicauta Gorhami* with 1% of cantharidin.

Cantharides in powder is adjusted to contain not less than 0.6% of cantharidin.

A study of *Cantharides* in practical pharmacognosy.—T. E. Wallis, *Pharm. J.*, ii/1927, 167.

**Antidotes.** Empty stomach by emetics or stomach tube. Medicinal charcoal, stirred up with a dose of magnesium sulphate, has been recommended. Give demulcent drinks freely, but *not* oils or fats. Morphine,  $\frac{1}{4}$  gr., hypodermically for pain. Hot baths or hot applications to the abdomen may relieve the pain.

**Uses.** Externally vesicant, irritant and powerful counter-irritant. Used in pleurisy, pericarditis, meningitis, neuritis, applied above the stomach to stop vomiting, and in rheumatoid arthritis (*v.* Emplastrum).

Internally is said to have aphrodisiac properties. Has been given in lupus and in chronic gout. Caution, avoid irritation of the kidneys. Hæmaturia is checked by 5-minim doses of tincture. It is of service in incontinence.

In cardiac dropsy cantharides is one of the most useful means of promoting diuresis. It acts on the secreting cells of the tubules, and the effects manifest themselves quickly. Dose of tincture may be 2, 3 or 10 minims according to age, given several times daily. Can usefully be added to a mixture containing caffeine, tincture of strophanthus and spirit of nitre.

[P1 81] **Ceratum Cantharidis** (*U.S.P. XI*)

Macerate cantharides 35 parts with a mixture of glacial acetic acid and turpentine, add to a melted mixture of beeswax, resin and benzoinated lard and heat to produce 1000 parts.

[P1 81] **Emplastrum Cantharidis** (*U.S.P. XI*)

Cantharides cerate 0.1 g. per sq. cm. of adhesive plaster, muslin, paper, or other suitable backing material

[P1 81] **Tinctura Cantharidis** (*U.S.P. XI*)

Average dose —  $1\frac{1}{2}$  minims (0.1 ml.).

Cantharides 10, glacial acetic acid 10, in alcohol to 100

[P1 81] **Mylabris** (*B.P.C.*). *Syn.* CHINESE CANTHARIDES

The dried beetles *M. Sida* and other species, some of which (*e.g.*, *M. pustulata*) may contain up to 2.3% of cantharidin. It is used as a source of cantharidin and as a substitute for cantharides in India and the East.

[P1 81] **Cantharidinum** (*B.P.*, *P. Ital. V*, *P. Helv. V*, *F.E. VIII*, *P. Belg. IV*).  $C_8H_{12}O(CO)_2O = 196.1$ .

**Dose.**—No dose in given in *B.P.* '32. *P. Helv. V* has max. single and max. daily dose approx.  $\frac{1}{320}$  grain.

Cantharidin is the lactone of cantharidic acid, in flat glistening rectangular prisms, melting at  $216^\circ$  to  $218^\circ$  and volatilising in very irritating white fumes. **Soluble** 1 in 55 of chloroform, 1 in 40 of acetone, 1 in about 1100 of alcohol 90%, and about 1 in 150 of acetic ether. Soluble also in ether, benzene, glacial acetic acid and fixed oils. Very sparingly soluble in water.

**Poisoning Effects and Antidotes**, see *Cantharis*.

**Uses.** Solutions of cantharidin, as well as other preparations of cantharides, are employed for stimulating the growth of the hair, in alopecia, and preventing its falling off.

[P1 81] **Acetum Cantharidini** (*B.P.C.*) contains cantharidin 1 in an acetic acid solution *q.s.* to 2000.

[P1 81] **Acetum Cantharidis** (B.P.C.). Cantharis, 1 in 10, extracted by percolation with an acetic acid menstruum.

[P1 81] **Collodium Vesicans** (B.P.C.) is a coloured solution of pyroxylin in blistering liquid

[P1 81] **Emplastrum Cantharidini** (B.P.). *Syn* BLISTERING PLASTER.

Contains cantharidin 0.2% in a basis of beeswax, castor oil and wool fat

[P1 81] **Emplastrum Calefaciens** (B.P.C.) contains 1 in 5000 of cantharidin.

[P1 81] **Emplâtre Mouches de Milan**, used in France, is similar

[P1 81] **Emplastrum Lyttæ** (B.P.C.). Powdered cantharides, 1 in 3, in a soft plaster basis

[P1 81] **Emplastrum Vesicans**.

Cantharidin 1, chloroform  $q\ s$ , heat to dissolve and add to yellow wax and wool fat, in equal portions, previously melted together, 499

[P1 81] **Linimentum Crinale** (*Squire*)

Cantharidin 1 gr., acetic ether 6 dr., dissolve with gentle heat, and add alcohol (90%) 6 oz., castor oil 2 oz., lavender oil 15 m. It is better to dilute this with an equal quantity of spirit, and the head should be washed after applying it a few times, to prevent the cantharidin accumulating

[P1 81] **Liquor Cantharidini** (B.P.C.). *Syn* TINCTURA CANTHARIDINI 1 in 10,000; is  $\frac{1}{8}$  strength of *I A* Dose.—2 to 5 minims (0.12 to 0.3 ml)

*Fr. Cx* and *P. Ital V* have 1 of cantharides in 10 of alcohol 70%. Max. single dose 9 minims, and max during 24 hours 25 minims approx.

[P1 81] **Liquor Epispasticus** (B.P.) contains cantharidin, 0.4% w/v, with castor oil and colophony in acetone. Should not be applied over too large a surface or toxic effects may occur from absorption.

[P1 81] **Lotio Cantharidini** (B.P.C.) *Syn*. LOTIO CRINALIS STIMULANS Cantharidin 1 in 5000 with acetone, castor oil and alcohol 90% (or methylated spirit).

[P1 81] **Oleum Cantharidatum** (*P. Jap IV*)

Macerate cantharides in powder 3, in olive oil 10, on the water bath for 10 hours with occasional shaking Strain.

[P1 81] **Unguentum Cantharidini** (B.P.C.).

Contains cantharidin 1, dissolved by means of chloroform in benzoated lard 3000.

One part diluted further with two of soft paraffin forms a useful pomade for stimulating growth of the hair.

Erasmus Wilson's [P1 81] **Unguentum Stimulans** is described as consisting of 1 of cantharides in 5 of plain lard.

[P1 81] **Unguentum Cantharidini cum Hydrargyro Compositum** is sold as "Pomade Max"

[P1 81] **Unguentum Hydrargyri Oxidi Rubri et Cantharidis** (W.H) Blistering liquid 15 m., red mercuric oxide ointment 1 oz.



**[P1-81] Potassi Cantharidas.** $C_{12}H_{17}O(COOK)_2 \cdot 2H_2O = 326.3$ . Fr. Cx. (+  $1H_2O$ ).

**Dose.**— $\frac{1}{100}$  to  $\frac{1}{200}$  grain (0.00015 to 0.0003 g.) hypodermically in very dilute solution. In minute white needles, soluble 1 in 25 of water. Has properties representative of cantharidin, *q.v.*

**CAOUTCHOUC***B.P.C., P. Helv. V.***India-Rubber.** *Syn.* ELASTICA.

The prepared milk-juice of *Hevea brasiliensis* (Euphorbiaceæ) and other species; known in commerce as pure Pará rubber.

**Preservation.** The best means of preserving rubber goods is to immerse completely in distilled water.

**Bandages of rubber.**—(i) Webbed with strands of rubber; (ii) Statham's porous; (iii) Martin's (solid) perforated and non-perforated, (iv) elastic circular stockings and india-rubber webbing.

**Bougies of solid elastic gum.**—

With bulbous end = à Boule, in sizes 1 to 16.

" " silk web " " " 1 to 16.

Conical pointed in shape " " " 1 to 12.

Cylindrical, not tapered, various textures and materials—sizes 1 to 16.

Œsophageal bougies are bulbous, conical and cylindrical, of elastic gum.—Sizes 10 to 24.

**Catheters.** Elastic gum, black and webbed, or silk web.—

Bulbous (à Boule).—Sizes 1 to 16.

Coudé (bent at end) also Bi-Coudé with two bends—Sizes 5 to 12.

Cylindrical.—Sizes 1 to 15, with or without wire stilettes, and sizes 5 to 12 with solid or hollow ends.

Conical (simply pointed, *i.e.*, tapered), with wire stilette.—Sizes 1 to 12.

**Catheters, Soft Rubber.**—13 and 16 inches long, with and without funnels, and the sizes vary between 4 and 12.

Belfast linen catheters are also prepared.

Web catheters may be sterilised by boiling in nearly saturated solutions of ammonium sulphate or sodium chloride, washing afterwards in sterile water.

**Catheters, Female,** are of glass, straight or curved, metal, or soft rubber.

**Dental Rubber,** manufactured of pure Pará rubber and coloured. This is supplied in various shades of colour, *e.g.*, white, pink, red, orange, black. The varieties in commerce are designated "Samson," "Doherty," "Gold Dust," Ash's "Whalebone," and Jamieson's "Horn." The rubber is hardened by vulcanisation and used to form a frame to carry artificial teeth. In vulcanising most rubber, especially Ash's, raise the temperature gradually until 315°F. or 100 lbs. pressure is obtained. Maintain this temperature or pressure 75 minutes to complete vulcanising process.

**Drainage Tubing** is of various dimensions, and is supplied in carbolised solution in glass tubes.

**Gloves, Surgical,** are prepared smooth and rough surface.

**Mackintosh or Waterproof Sheetting,** 36 and 54 inches wide is supplied having rubber on one or both sides.

**Pessaries** are ball shape, butterfly, circular, oval, cradle and ring form.

**India Rubber Plasters** are made 7 inches wide and in tape form.

**Stomach Tubes.** That known as Van Valsh's, with bevelled "Velvet Eyes," is considered one of the best, but the bevelling may have the disadvantage of weakening the tube on one side and causing it to turn round when an obstruction is met. For passing the tube a special lubricant jelly is supplied, or a glyco-gelatin pastille of menthol and cocaine is useful.

**Sutures** (*vide* Ligatures).

**Emplastrum Adhesivum (B.P.C.)** is spread with a rubber adhesive compound containing not more than 25% of fillers.

**Ligamentum Elasticum Adhesivum (B.P.C.)** is spread with a rubber adhesive plaster containing not less than 20% of zinc oxide.

**Elastoplast Bandages** (*T J Smith & Nephew, Hull*) Self-adhesive, resilient elastic plaster bandages, available in various widths and lengths

These bandages have been much used as a tight binder for varicose veins and ulcers, both for support and for fixing zinc gelatin dressings

They also provide compression and support for the after-treatment of fractures and dislocations, injuries to joints, tendons, muscles, etc., fracture of ribs, clavicle, femur, Colles' fracture, etc.

X-ray photographs can be taken through several layers of Elastoplast

**BED-SORES.** Ten cases successfully treated, the dressing being left on as long as it would adhere, and then replaced with fresh dressing, no attempt being made to clean the surface of the sore. Fifteen days the longest time taken for healing.—*T J. A. Carty, Brit. med. J.*, 1/1935, 105

**BOILS.** Twenty cases successfully treated by the occlusive method. The dressing used was Elastoplast bandage applied directly to the shaven skin and extending well beyond the outer limit of the inflamed area, the surrounding skin being sterilised with 1 1000 acriflavine solution. The average number of dressings was 2 or 3 and the average days under treatment 11 or 12.—*P. K. Fraser, Brit. med. J.*, 11/1935, 894.

**IMPETIGO.** Treatment by occlusive dressing consisting in the application of a piece of Elastoplast bandage to the lesion without cleaning adjacent skin, removing crusts or pricking pustules, and leaving the bandage in situ. Total time lost by school children 9 7 days per child, compared with 18 6 days by Ung. Hyd. Ammon. Dil. treatment and 22 5 days by intensive ointment treatment and removal of crusts by starch poultices. Results better and infectivity of the disease diminished.—*J. L. Newman, Brit. med. J.*, 1/1933, 823. Confirmation—*J. M. Morris, ibid.*, 986

**VARICOSE ULCERS.** Put the hydraulics right and the ulcer will take care of itself. The varicose circulation should be squeezed out of existence. The ulcers should be hermetically sealed with sticking plaster, as found by Bayton 150 years ago. In technique 5% sodium morrhuate injection and a 3-inch Elastoplast bandage. Discharge occurs and is beneficial. Enormous cost of patients of this kind to the State. Some probably £5,000 each. 324 patients cured.—*A. Dickson Wright, Brit. med. J.*, 11/1930, 996. See also "Chronic ulcer of the leg treated by Dickson Wright Method." There is no danger of putting the bandage on too tight, and no danger of imprisoning septic secretions of the foulest.—*J. H. Twiston Davies and A. E. Drynan, Brit. med. J.*, 11/1930, 998

Reflux pressure in the veins may upset the hydraulics on removing bandage, Single long veins easiest to treat.—*F. A. E. Silcock, Brit. med. J.*, 1/1931, 34

Varicose ulceration. Compression or squeezing of excess fluids out of the limb. Very tight bandaging required.—*J. H. Twiston Davies, Brit. med. J.*, 1/1931, 201.

Support is given which skin and tissues have lost and the blood is made to circulate properly. Patients should walk about.—*Sir L. Hill, Brit. med. J.*, 1/1931, 240.

Method beneficial.—*H. Haldin-Davis and others, Brit. med. J.*, 1/1931, 329, 330.

Painting the leg with 5% ichthylol in glycerin prevents irritation.—*R. W. Cockshut, Brit. med. J.*, 1/1931, 652.

**WARTS.** A simple and effective treatment for warts on the hands is to bind the warty parts tightly with Elastoplast, which is removed once a week, the softened epithelial debris being scraped away with a blunt scalpel.—*McAusland, Brit. med. J.*, 1/1935, 1123.

**Liquor Caoutchouc (B.P. '98).** Caoutchouc 1, benzene 10, carbon disulphide 10. Treat the rubber with the carbon bisulphide for an hour or two to form a jelly, and add the benzene. It may be medicated, but traumaticin is preferable.

**Gutta Percha (B.P.C.).**

The dried purified latex of *Palaequium oblongifolium* and other species (Sapotaceæ). Occurs in lumps, brownish externally, reddish-yellow or reddish-grey internally, and consists chiefly of the hydrocarbon, gutta ( $C_8H_8$ )<sub>n</sub>.

The principal districts of supply are Pahang, Kelantan, Siak, Bolungen and Sarawak. Small quantities are also exported from Siam and Manila, and a lower grade from Nigeria. From Borneo is obtained the well-known "leaf gutta"; this is extracted from the leaves and small twigs of the tree, and is boiled, cleaned, and pressed into slabs and cakes, considered by some to be the best. Unfortunately on keeping it oxidises and becomes brittle. Gutta percha is the balata of the old world, as balata is the gutta percha of the new world.—*Chem. & Drugg Commercial Compendium*

[P1] **Liquor Gutta Percha (B.P.C.)** *Syn* TRAUMATICIN Gutta percha 10% w/v in chloroform *P. Belg.*, *P. Ital V*, *F.E. VIII* and *P. Ned V* use gutta percha (purified) 1, chloroform (by weight) 9. More cleanly than liniments or ointments.

**Tela Gutta Percha (B.P.C.)** Gutta percha tissue is gutta percha in thin sheets.

**Sericum (B.P.C.). Silk**

The prepared fibre from the cocoons of the silkworm, species of *Bombyx* and of *Antheræa*. The fibre is unwound from the cocoons and degummed. The threads are solid and rounded or rounded-triangular in cross-section. They are soluble in 5% aqueous potassium hydroxide

**Sericum Oleatum (B.P.C.). Oiled Silk.**

A silk fabric made waterproof by treatment with a drying oil, often coloured with a green dye.

**Sindon Oleata (B.P.C.) Oiled Cambric** *Syn.* YELLOW OILED CAMBRIC

A bleached cotton cloth made waterproof by treatment with a drying oil

**CAPSICUM***B.P.*

*Syn.* CAYENNE, AFRICAN PEPPER, CHILLIES, CAPSICI FRUCTUS.

*Dose.*— $\frac{1}{2}$  to 2 grains (0.03 to 0.12 g.), in a pill.

The dried ripe fruit of *Capsicum minimum* (Solanaceæ). Capsicum (*U.S.P. XI*) is from *C. frutescens* with 12% ether-soluble and non-volatile extractive. Capsicum (*P. Helv. V*, *P. Dan.*) is from *C. annuum* var. *longum*

Contains as chief constituent capsaicin,  $C_{18}H_{27}O_3N$ , the average content being about 0.14%.

**Emplastrum Capsici (B.P.C.).** Contains 1 in 50 of oleoresin of capsicum in plaster of colophony.

**Emplastrum Capsici Elasticum (B.P.C.)** is the same strength as the preceding but is made with rubber adhesive plaster.

Capsicum plasters in rubber combination are also made in sheets 7 in. by 5 in., and yard rolls 7 in. wide.

**Emplastrum Capsici Mitis (R.D.H.).**

Caoutchouc 10, yellow soft paraffin 1; heat carefully so as just to liquefy and add colophony 10, orris 4, capsicum, finely powdered, 4. Spread thinly on holland or linen and cut into pieces half the size of a finger-nail.

**Emplastrum Capsici Fortis (R.D.H.)**

Prepare as above, omitting the capsicum. When spread, brush the surface with a thin coating of compound capsicum oleoresin ointment (B.P.C.).

These plasters are for dental use.

**Fluidextractum Capsici.**

*Dose*.—1 minim (0.06 ml). Alcoholic percolate, 1 = 1. Gerrard advised the following formula.—

Exhaust capsicum 100 with 90% alcohol, distil off alcohol until the residual extract weighs 50, 1 of extract = 2 of drug.

**Gossypium Capsici (B.P.C.).** *Syn.* CAPSICUM WOOL, CALORIFIC WOOL. Contains the equivalent of about 20% of capsicum.

Alternative formula (Gerrard).—

Dissolve liquid extract of capsicum (Gerrard) 2 oz. in alcohol 90% 7 oz. Pour the solution on to the cotton wool 9 oz. under pressure to saturate evenly. Dry and preserve in well closed cartons. Contains 10% extract. Colour with eosin, as otherwise the colour fades. Cover with oiled silk when applying, to increase activity.

**Linimentum Capsici (B.P.C.).**

Stronger tincture of capsicum about 1 in 3, with oleic acid, oil of lavender and alcohol.

Painted on the skin, or applied sprinkled on piline or flannel, it produces a red glow within one hour; its action may be arrested by smearing the part with soft paraffin. Useful in chest affections, rheumatism, sciatica, etc. Does not redden the skin for any length of time, hence may be used on exposed parts.

**Mistura Capsici Sedativa (L.H.)**

Potassium bromide 10 gr., sodium bicarbonate 10 gr., tincture of capsicum 5 m., strong tincture of ginger 5 m., infusion of quassia to  $\frac{1}{2}$  oz. For alcoholic dyspepsia.

**Oleoresina Capsici (B.P.C.)** *Syn.* CAPSICIN

*Dose*.— $\frac{1}{100}$  to  $\frac{1}{30}$  grain (0.0006 to 0.002 g.).

Made by extracting with ether, and evaporating the solvent, extracting the residue with alcohol 90% and removing the alcohol by evaporation. It is approximately four times as strong as the oleoresin of the B.P.C. 1923, and occurs as a dull reddish-brown oily mass becoming crystalline.

Commercially, so-called oleoresins are also available, consisting of the extractive obtained by percolation with ether or with acetone.

**Pilula Capsici Composita.**

Capsicum oleoresin  $\frac{1}{2}$  m., clove oil  $\frac{1}{2}$  m., calomel 1 gr., aloe 2 gr. For the atonic stomach of drunkards.

The proportion of oleoresin should be reduced owing to the increased strength of the B.P.C. 1934 preparation.

**Tela Carbasi et Gossypii Capsici (B.P.C.).** *Prop. Names.* THERMOGENE (*Thermogene Co., Hayward's Heath*), CAPSOGEN (*Southall Bros. & Barclay, Birmingham*). Capsicum tissue consists of capsicum wool enclosed in absorbent gauze.

**Tinctura Capsici (B.P.).**

*Dose.*—5 to 15 minims (0·3 to 1 ml.).

1 in 20 of 60% alcohol.

Given internally it increases the flow of saliva and gastric juice. Increases peristalsis, relieves atonic dyspepsia, and is useful in dipsomania—it allays the craving for alcohol (*cf.* *Mistura Capsici Sedativa*). The *B.P.* tincture is too weak for external use as a rubefacient.

**Tinctura Capsici (U.S.P. XI).** *Average dose.*—8 minims (0·5 ml.). 1 in 10

**Tinctura Capsici Ætherea.**

Prepared as *B.P.* tincture, with ether instead of alcohol.

**Tinctura Capsici Fortior (B.P.C.).** *Syn.* TURNBULL'S TINCTURE OF CAPSICUM.

*Dose.*—1 to 3 minims (0·06 to 0·2 ml.). 1 in 3. Principally used externally. Is useful for chilblains, but only when the skin is not broken. This is too irritating generally.

**Unguentum Capsici (B.P.).**

Capsicum, bruised, 25% in a basis of soft and hard paraffins and lard, strained after digesting an hour on the water bath.

[P1] **Unguentum Capsici Compositum (B.P.C.)** *Syn.* UNGUENTUM OLEORESINÆ CAPSICI COMPOSITUM, CHILLIE PASTE.

Oleoresin of capsicum 2%, with menthol, chloral hydrate and camphor in yellow soft paraffin.

**Unguentum Capsici Forte (B.P.C.).**

Oleoresin of capsicum 4·5% in yellow beeswax and benzoinated lard. May be too strong for tender skins—will bear dilution 2 or 3 times.

**Capsolin (Parke, Davis, London).** Camphor, capsicum and turpentine in ointment form for use as external counter-irritant to counteract local congestion, muscular rheumatism, neuralgia, etc

**Arnicae Flos (B.P.C.).**

The dried flowerheads of *Arnica montana* (Compositæ). Gastric and intestinal irritant.

**Antidotes.** Give emetic if patient has not already vomited. Medicinal charcoal, stirred up in water, may be given freely, also demulcent drinks.

**Tinctura Arnicae Floris (B.P.C.).** *Dose.*— $\frac{1}{2}$  to 1 fl. drachm (2 to 4 ml) 1 in 10. Sometimes used as an application for sprains and bruises, but may produce severe dermatitis. Under saline purges and sedative ointment rash and irritation subside.

**Arnicae Rhizoma (B.P.C.).** *Syn.* ARNICA ROOT.

The dried rhizome and rootlets of *A. montana* (Compositæ).

**Linimentum Arnicae (B.P.C.).** *Syn.* ARNICA OPODELDOC.

A solid liniment containing 1 in 4 of tincture of arnica root in a soap basis

**Tinctura Arnicae Radicis (B.P.C.).** *Syn.* TINCTURE OF ARNICA. 1 in 20.

**Calendula (B.P.C.).** *Syn.* MARIGOLD FLOWERS. Dried florets of *Calendula officinalis* (Compositæ).

**Tinctura Calendulae (B.P.C.).** 1 in 5 of alcohol 90% *Dose.*—5 to 20 minims. Applied to sprains, diluted with 20 to 30 parts of water, and given in amenorrhœa. It has diuretic and stimulant properties.

[P1-81] **Cevadilla (B.P.C., P. Helv. V, P. Dan.).**

*Syn.* SABADILLA, CAUSTIC BARLEY.

[P1] "*Alkaloids, the following; their salts, simple or complex.—Sabadilla, alkaloids of.*"

[S1] "*Alkaloids, the following; their salts, simple or complex.—Sabadilla, alkaloids of, except substances containing less than 1% of the alkaloids of sabadilla.*"

[S6] "*Alkaloids—sabadilla, alkaloids of—specify proportion as the proportion of any one alkaloid of sabadilla that the preparation would be calculated to contain on the assumption that all the alkaloids of sabadilla in the preparation were that alkaloid.*"

The dried ripe seeds of *Schœnocaulon officinale* (Liliaceæ), containing the alkaloid cevadine (*syn.* veratrine, which name has also been given to veratridine, an amorphous alkaloid, and to indefinite mixtures of cevadine and veratridine).

Used as a parasiticide, especially for pediculi capitis, in the form of [P1 S1] ointment 20% or as—

[P1 S1] *Acetum Cevadillæ* containing 10 of cevadilla macerated in alcohol 10, acetic acid 17.5 and water to 100.

[P1 S1] **Veratrina** (*B.P.C.*, *P. Helv. V*, *P. Ned. V*). *Syn.* AMORPHOUS VERATRINE.

A mixture of alkaloids from cevadilla containing cevadine (crystallised veratrine),  $C_{27}H_{49}O_9N$ , veratridine,  $C_{27}H_{53}O_{11}N$ , cevadilline,  $C_{34}H_{53}O_8N$ , sabadine,  $C_{29}H_{51}O_8N$ , and cevine,  $C_{27}H_{49}O_9N$ . It occurs as a whitish or greyish powder with bitter taste followed by numbness of the tongue. **Soluble** about 1 in 3 of alcohol 90%, 1 in 6 of ether, 1 in 3 of chloroform and in other organic solvents, also in acids, forming salts.

**Antidotes.**—If patient has not vomited freely, empty stomach by emetic or stomach tube. Give medicinal charcoal, stirred up in water. Keep patient warm, lying down with head rather lower than the rest of the body. Stimulants, *e.g.*, aromatic spirit of ammonia  $\frac{1}{2}$  dr. in water by mouth, or hot, strong coffee by rectum. Atropine,  $\frac{1}{100}$  gr., hypodermically.

**Uses.** Is applied externally, where the skin is not broken, for its analgesic properties in neuralgia.

**Caution.**—Its sternutatory properties are most marked.

[P1 S1] *Oleinatum Veratrinæ* (*B.P.C.*) 2% w/w in oleic acid and olive oil.

[P1 S1] *Unguentum Veratrinæ* (*B.P.C.*) 2% in oleic acid and benzoinated lard.

[P1] **Veratrum Album** (*B.P.C.*, *P. Helv. V*) *Syn.* WHITE HELLEBORE RHIZOME.

[P1] "*Alkaloids, the following; their salts, simple or complex.—Veratrum, alkaloids of.*"

[S1] "*Alkaloids, the following; their salts, simple or complex.—Veratrum, alkaloids of, except substances containing less than 1% of the alkaloids of veratrum.*"

[S6] "*Alkaloids—veratrum, alkaloids of—specify proportion as the proportion of any one alkaloid of veratrum that the preparation would be calculated to contain on the assumption that all the alkaloids of veratrum in the preparation were that alkaloid.*"

The dried rhizome and roots of *V. album* (Liliaceæ). Contains jervine, protoveratrine and other alkaloids. Formerly used internally in dropsy and externally as a parasiticide.

[P1] **Veratrum Viride** (B.P.C., U.S.P. XI). *Syn.* AMERICAN HELLEBORE, GREEN HELLEBORE RHIZOME.

*Dose*—U.S.P. XI average dose  $1\frac{1}{2}$  grains.

The dried rhizome and roots of *V. viride* (Liliaceæ). Contains various alkaloids as in white hellebore. Is a powerful cardiac, nerve and arterial sedative, useful in puerperal eclampsia, hyperpiesia and in aneurism.

Both the preceding must be distinguished from *Helleborus Niger* (Ranunculaceæ), or Christmas Rose, which is purgative and emmenagogue and has strong sternutatory properties. It is now little used.

*H. niger* and *H. viride*—a comparative study. It is not possible at present to find any character enabling one to distinguish with certainty between these rhizomes and roots.—T. E. Wallis and A. M. Saunders, *Pharm. J.*, ii/1924, 90.

[P1] **Tinctura Veratri** (B.P.C.). *Dose*.—5 to 30 minims (0.3 to 2 ml.). 1 in 10.

[P1] **Tinctura Veratri Viridis** (U.S.P. XI).

*Average dose*.—15 minims (1 ml.). 1 in 10.

[P1] **Veratrone** (Parke, Davis, London). An extract of veratrum 1 ml. of which is equivalent to 20 minims of tincture. In eclampsia

**Piper Nigrum** (B.P.C.). *Syn.* PIPER. *Dose*.—5 to 10 grains (0.3 to 0.6 g.)

The dried unripe fruits of *Piper nigrum* (Piperaceæ). Contains 5 to 9% of the alkaloid piperine and 1 to 2.5% of volatile oil.

Black pepper has stimulating, carminative and diuretic properties

**Piper Album** is black pepper fruits from which the outer coatings have been removed. It contains less volatile oil than black pepper.

**Piper Longum**. *Dose*.—5 to 10 grains (0.3 to 0.6 g.) is the dried unripe fructification of *P. Chaba* (Piperaceæ). Contains about 5% of piperine and 1% of volatile oil.

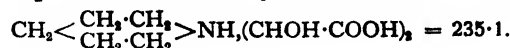
**Confectio Piperis** (B.P.C.). Black pepper 10% with caraway and purified honey.

**Piperina**.  $C_{17}H_{19}O_3N = 285.2$ . *Dose*.—1 to 10 grains. A crystalline principle from the fruits of *Piper nigrum* and *Piper longum* (Piperaceæ). Melts at  $130^\circ$ . Insoluble in water, soluble in alcohol. It has febrifuge, stomachic and antiperiodic action.

**Oleoresina Piperis**. *Average dose*.— $\frac{1}{4}$  grain. Is prepared by acetone extraction of pepper.

**Piperidine**, *syn.* HEXAHYDROPYRIDINE,  $C_4H_{11}N$ , is a colourless liquid with peppery odour and taste; b.p.  $106^\circ$ .

**Piperidinæ Tartras**. *Syn.* PIPERIDINE ACID TARTRATE.



*Dose*.—10 to 15 grains (0.6 to 1 g.).

Colourless pleasant-tasting crystals, readily soluble in water. Uric acid solvent.

**Effervescent Piperidine Tartrate**.

*Dose*.—1 drachm or more; 5 grains in 1 drachm.

## CAPSULES

Capsules are made with a gelatin base and varying quantities of glycerin according to the degree of flexibility required. They are used for a variety of medicaments and are particularly suitable for nauseating oils. Soft gelatin capsules may be used for both liquid and solid medicaments, but it is unusual to put liquids into the hard type of gelatin capsule. Soft capsules are obtainable in various sizes having capacities of 3, 5, 10, 15, 20, 30, 60 and 90 minims. Hard capsules are obtainable in sizes which will hold 3, 4, 5, 6, 8, 10, 15, 25 gr. of sodium bicarbonate. A special form of soft gelatin capsule, made and filled by machinery, is known as a "perle."

Soft capsules are to be preferred to the hard variety because they are more easily swallowed. Aqueous liquids tend to soften the capsule and should not, therefore, be prescribed in such containers. If it is necessary to include them, they should either be evaporated to low bulk and mixed with almond oil or they should be emulsified in almond oil using a little wool fat or white wax as emulgent.

Liquids such as creosote and various volatile oils may cause discomfort in the stomach if dispensed undiluted in capsules. They should be mixed with four times their volume of almond oil and then capsuled.

### Glutoid (Enteric) Capsules

These may be hard or soft gelatin capsules and are intended to pass unchanged through the stomach and dissolve in the intestines. For this purpose they should be filled and sealed in the usual manner, then immersed for 5 minutes in solution of formaldehyde diluted with three times its volume of water and afterwards dried. Variable results may be obtained owing to variation in the composition of the capsule base. The action of the formaldehyde on the gelatin varies with the time of immersion and the amount of gelatin present. Moreover, the hardening effect of formalising increases on keeping and they should, therefore, be freshly prepared. The finished capsules may be tested in the following manner. They should not dissolve in an aqueous solution of glycerin of pepsin and hydrochloric acid when immersed for two hours at 37°, but should dissolve in an alkaline pancreatin solution at the same temperature.

Glutoid capsules are useful for (a) drugs which may be inactivated in the stomach such as pancreatin or ox bile; (b) drugs which are more efficacious if they reach the intestines in a concentrated form, such as anthelmintics, intestinal disinfectants, and drugs like emetine and emetine bismuth iodide.

**Slipules** (*Martindale, London*), and **Pulvules** (*Lilly, London*) are hard gelatin capsules of the "slipover" variety.

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## CARBO

*B.P.C., P. Dan.**Syn.* CARBO LIGNI, MEDICINAL CHARCOAL.*Dose.*—1 to 2 drachms (4 to 8 g.).

Made by burning wood, *e.g.*, willow, with access of as little air as possible.

In cachets or as charcoal biscuits as an adsorbent in distension of the stomach, *e.g.*, in dyspepsia. Is antiseptic, and is used externally as a poultice to foul ulcers. COCA NUT CHARCOAL was employed by Dewar owing to its remarkable powers of absorbing gases to improve high vacua.

A test of activity of medicinal and other charcoals by exposure to water and other vapours. Active charcoal will absorb 50 to 100%, or even more, of moisture. The water figure is slightly higher than that for alcohol or turpentine. *Pulv. Carbo. Lig.* as ordinarily dispensed for medicinal purposes is *inactive*. The author suggests improvements in the manufacture and the adoption in the *B.P.* of tests for activity.—H Brindle, *Pharm. J.*, 11/1928, 84.

It has been calculated that 15 grains of medicinal charcoal can absorb *in vitro* 13 gr. of corrosive sublimate, 20 gr. of iodine, 9 gr of strychnine, 4.5 gr. of phenol from 1% solution, 8 gr. of potassium permanganate.—G. H. W. Lucas and V. E. Henderson, *Canad. med. Ass. J.*, 11/1933, 22.

*Cataplasma Carbonis (B.P.C.)* 10% in linseed poultice.

**Carbo Activatus** (*B.P.C., U.S.P. XI*). *Syn. and Prop. Names* DECOLOURISING CARBON, NORIT (*Norit, Amsterdam*; *C. Zimmermann, London*). CARBOSERIN (*Bayer Products, London*) is activated charcoal in tablet form.

*Dose.*—As for Carbo.

Prepared by heating charcoal to a high temperature in a stream of steam or other activating gas (by which its adsorptive power is greatly increased), washing and drying. *U.S.P. XI* states that Carbo Activatus may be dispensed when Carbo Ligni is prescribed.

Activated charcoal adsorbs or inactivates strychnine, brucine, adrenaline, histamine and tyramine. With ephedrine and acetylcholine adsorption or destruction is not quite complete.—F. Saunders and co-workers, *J. Pharmacol.*, June, 1931, 177.

**Carbo Animalis** (*B.P.C.*) is prepared by boiling crude animal charcoal with hydrochloric acid, washing and drying. *P. Helv. V* describes Carbo Adsorbens, Carbo Adsorbens Granulatus and Carbo Ligni; the first must be dispensed when Carbo Animalis is prescribed.

**Intravenous Injections in Infective Conditions.**—Over 100 patients treated, including 14 cases of acute puerperal infection, 5 of pneumonia, 3 of acute cholecystitis, and 5 of furunculosis. No reaction, and all patients recovered. Initial dose 3 ml. of a 2% suspension of finely pulverised animal charcoal, the piston of the syringe, and the needle, being lubricated with liquid vaseline to prevent jamming.—E. Saint-Jacques (Montreal), *Lancet*, 1/1934, 418.

Doses consist of 2 to 5 ml. of a 1 to 3% suspension of charcoal in isotonic glucose serum, injections being given daily, or every other day, or at longer intervals, the maximum total dosage being 42 ml. of a 2% solution. Injections painless, free from violent or febrile reaction. Best results in diffuse inflammatory processes when reaction of the organism to the infection hangs fire, or when it runs an acute and serious course without free suppuration.—Gaudier and Demarez, *Bull. Acad. méd., Paris*, 1934, 112, 45.

**ERYSIPELAS.** Intravenous injections of 3 to 5 ml. of a 2% suspension of animal charcoal in a 10% hypertonic dextrose solution bring about a rapid process of recovery—the pain and tension stop, the fever abates and then disappears, the erysipelatous patches lose their lustre and regress, general symptoms improve, and desquamation rapidly takes place.—H. D. Gonzalez and M. Scheingart, *per J. Amer. med. Ass.*, i/1936, 1430.

**Carbonacid** (*Richter, London*). Charcoal containing 2% of HCl. *Dose*.—2 tablets 3 times daily with meals. In flatulent dyspepsia, etc.

**Carbonactyl** (*Pharmaceutical Specialities (May & Baker) Ltd., London*) 2% aqueous suspension of animal charcoal for intravenous use. Ampoules contain 5 ml. For acute infections—pneumonia, gonococcal epididymitis, etc.

**Carbonei Dioxidum** (*B.P., U.S.P. XI*). *Syn.* CARBONIC ANHYDRIDE.  $\text{CO}_2 = 44$ .

Carbon dioxide in the gaseous condition when used in dilutions of 4 to 6% with oxygen stimulates expiration, acts as a cardiac stimulant, exerts an indirect effect as a sedative and tones up a weak pulse. It has been used after an anæsthetic and operation, in pneumonia and in asphyxia from other causes, *e.g.*, electric shock and drowning.

It has also been inhaled in ozæna and nasal catarrh. It is believed to act as an antiseptic in such cases.

To accelerate pulmonary elimination of poisons or drugs, *e.g.*, carbon monoxide, ether and alcohol.

**ACUTE ALCOHOLISM.** Acute alcoholic coma with dangerous respiratory depression, paralysis and cyanosis is a medical emergency. Death may be definitely prevented and recovery accelerated by inhalation of a mixture of 10% carbon dioxide in 90% oxygen for a length of time sufficient to maintain normal respiration and colour, even after the inhalation is suspended. A minimum time of half an hour should be observed. If necessary, the inhalation may be carried out longer.—L. J. Robinson and S. Selesnick, *J. Amer. med. Ass.*, ii/1935, 1735.

**ANÆSTHESIA.** In general anæsthesia as an aid.—J. S. Lundy, *J. Amer. med. Ass.*, ii/1925, 1953.

Carbon dioxide and oxygen to prevent atelectasis. Important prophylactic in operations—La Flèche, *Brit. med. J.*, ii/1930, 526.

Carbon dioxide 5% (some employ even 25%) with oxygen as a control of respiration in anæsthesia; also in asphyxia of the new-born, alcoholic intoxication and carbon monoxide asphyxia. The mixture is not used "straight" but is added to air or oxygen from another cylinder.—Yandell Henderson, *Brit. med. J.*, ii/1925, 1170. *See also ibid.*, 1181 *et seq.* and 1186.

**ANGINA PECTORIS** benefited by inhalation daily for 15 minutes from an open mask.—*Brit. med. J. Epit.*, ii/1931, 26.

**PNEUMONIA.** In the absence of respiratory failure, as evinced by shallow breathing, the clinical benefits of  $\text{CO}_2$  administration are not sufficiently demonstrated to warrant its routine use in lobar pneumonia.—R. Hilton, *Brit. med. J.*, i/1934, 420.

**WHOOPIING COUGH.** Dyspnoea and cyanosis immediately relieved in a child of 8 weeks by spraying a little gas on the face.—J. Dunlop, *Brit. med. J.*, ii/1932, 822. Also in spasmodic asthma and chronic rhinitis.—G. Willett, *ibid.*, 1996.

**"Carbonic Snow,"** *i.e.*, carbon dioxide in the semi-solid condition, formed as the gas evaporates from a storage cylinder, is much employed therapeutically. The cylinders contain  $\text{CO}_2$  at a pressure of about 950 lbs. to the square inch (65 atmospheres), yield the snow on opening with a temperature of  $-79^\circ \text{C}$ . ( $-110^\circ \text{F}$ .), which by collecting in a suitable receptacle can be formed into a stick or crayon like an ordinary candle, or may be compressed into a mould and cut any shape with a knife. The

cylinders should be mounted on a stand with the stopcock on a lower level than the opposite end so that the liquid gas covers the inner orifice of the valve.

**Crayons, Method of Making.** The snow evaporates slowly—a crayon 5 by 1 inch will last about 1 to 2 hours. As many as thirty applications with this size can be made. The temperature of the crayon is *constant*. A towel is folded into three and wrapped round an ordinary ruler—the ruler is then removed and the tube thus produced is bound on to the valve of the CO<sub>2</sub> cylinder, the gas is turned on and the towel tube fills with the snow. The frozen gas may then be pressed into a piece of vulcanite or celluloid tubing about 1 inch in diameter with a ruler. A cardboard postal tube or roll of blotting paper (several thicknesses) will also serve. Cover end of crayon with lint for handling. Can be pointed with a pen-knife or shaped by rubbing against the side of a vessel containing hot water.

An old glove finger has been suggested for collecting the CO<sub>2</sub> by tying on to the vent of the cylinder. When completely filled and rigid, remove and with a sharp knife cut the end of the finger off at about 1½ inches from the point, thus exposing a corresponding length of the crayon, which can be used to the part, the rest of the glove finger serving as a holder.

**Uses.** For removal of *nævi*, moles and blemishes, lupus erythematosus, lupus vulgaris, rodent ulcer, and warts (for last mentioned long application necessary). Also employed for trachoma and chronic localised eczema. A single application usually suffices. The thawing out is usually more painful than the freezing.

**ALOPECIA AREATA** of 3 to 7 years' duration well treated. Hair grew after three or four applications within 3 weeks.—*Per J. Amer med. Ass.*, ii/1925, 552. *See also Prescriber*, 1926, 35.

**CORNEAL ULCERS.** The surface of the ulcer is carefully touched. Cocaine is not necessary. If patient complains of discomfort the eye can be bathed with cold boracic lotion. The surface of the ulcer becomes white and raised, within 24 or 36 hours this "slough" separates, leaving a clean healing ulcer. Infiltrations disappear from the surrounding healthy cornea and hypopyon vanishes. After treatment, pads and bandages are used instead of fomentations, and atropine sulphate 1% is instilled once daily. The method is not advised for marginal or ring ulcers.

**KERATOSIS** accompanying X-ray dermatitis. Brief applications answer well. The treated area becomes firmer and in 2 or 3 minutes swollen. A wheal forms with acute hyperæmia within half an hour and a vesicle usually within an hour, applying 30 seconds or longer, this will almost certainly be followed by scarring. An intense superficial destruction is obtained by a second application immediately after the tissues have thawed out.

Boric ointment is used for after-treatment. If blister forms, the fluid is removed within a few days; the crust forming should be allowed to fall off. The scar ultimately is pale, soft and pliable.

**NÆVI.** In the case of an ordinary capillary *nævus* the crayon is roughly shaped to that of the *nævus*—or slightly larger; it is applied and firmly pressed down for, on an average, 40 seconds. If there is bone immediately beneath, a shorter time will do. For a cavernous *nævus* the end of the crayon is made the same size or slightly smaller than the area of the growth. A long application with deep pressure should effectually freeze the whole mass.

The treatment of strawberry *nævi* with CO<sub>2</sub> snow.—H. C. Semon, *Lancet*, i/1934, 1167.

**ORIENTAL SORE** Perseverance is necessary as there is strong tendency to recur.

**PSORIASIS.** Patches removed by 30 seconds' application.

**RODENT ULCER.** Early rodent ulcers up to the size of a shilling treated as follows:—

Ring the ulcer with Novocain 2% and firmly scrape with a sharp spoon; the tumour comes away and a clean raw area is left. Apply a pencil of  $\text{CO}_2$  snow for 60 seconds and then a dry dressing. There is œdema for a day or two but practically no pain, and the ulcer heals rapidly under boric ointment. The resulting scars are very smooth and fine. Recurrences infrequent and successfully treated by a repetition.—J. F. Smith, *Brit med J*, 11/1928, 443.

Although it has occasionally cured a case, its use on the whole is most unsatisfactory. It is painful and produces scarring, and the proportion of failures is too great to make it permissible to use it.—N. S. Finzi, *Brit med J*, 11/1933, 137.

**TRACHOMA.** The method may be applied energetically in trachoma without risk. The lid is everted and separated from the globe by a non-conducting spatula—the pencil is lightly pressed down on to the part of the conjunctiva to be treated for 15 to 30 seconds.

**Carbonei Disulphidum** (*B.P.C., P. Helv. V*). *Syn.* CARBON BISULPHIDE.  $\text{CS}_2=76.12$ . A clear liquid with characteristic odour, sp. gr. 1.268 to 1.272. Almost insoluble in water but readily in alcohol, ether and chloroform and the fixed and volatile oils. Dissolves phosphorus, sulphur and rubber with avidity.

**Antidotes.** Keep patient in bed and warm. Oxygen inhalations if necessary.

**CHRONIC POISONING** in industry. Absorption takes place both through the lungs and the skin, and the poison is cumulative. A concentration of 1 in 3000 in air will produce a headache after a few hours exposure.—Memorandum on precautions against dangers of poisoning, fire, and explosion associated with the use of carbon bisulphide in artificial silk, india-rubber, and other works.—H.M.S.O., Form 836, 1936.

With continued exposure there is impairment of memory and mental depression, with possible weakness of the facial muscles and flexor muscles of the forearms.—*Brit med J*, 1/1934, 998.

**Uses.** In tuberculosis it is useful when inhaled, and has no disagreeable after-effects. In fibrinous pneumonia small doses with water have been used.

**DIARRHŒA.** Has been used as a remedy for diarrhœa in doses of 30 ml. of a 3.5% solution 4 to 5 times a day.—J. W. Tomb, *Brit. med J*, 1/1934, 1097.

## CHLORINATED HYDROCARBON COMPOUNDS.

**Carbonei Tetrachloridum** (*B.P., U.S.P. XI, P. Ned. V, F.E. VIII*). *Prop. Name* TETRAFORM (*British Drug Houses, London*).  $\text{CCl}_4=153.83$ .

**Dose.**— $\frac{1}{2}$  to 1 drachm (2 to 4 ml.). 6 ml. doses have been taken by an adult. 10 to 20 minims is safe for children of 3 to 4 years. Children of 1 year can have 10 minims; a child of 10 should receive 30 minims; a youth of 16, 40 minims ( $2\frac{1}{2}$  ml.), and so on even when seriously ill from various causes. *U.S.P. XI* average dose (caution) 40 minims. *Milk* is the best vehicle even if given in capsule. Must not be given in spirit or turpentine.

Not the ideal anthelmintic. In addition to the many deaths reported in the literature (some with doses as low as  $1\frac{1}{2}$  ml.) there are many unreported fatalities. No justification in morality, science, or expediency in the "herd" treatment of backward races.—Clayton Lane, *Brit. med J*, 11/1928, 195.

See also *Lancet*, 1/1930, 1817. 1.5 ml. is the fatal dose. Very strong remarks repeated.

A heavy, volatile, and mobile chloroform-like liquid, has a pleasant, pungent, quince-like odour if pure.

**Antidotes.** (Swallowed.) Empty stomach by emetic or stomach tube. Keep patient lying down and warm. Give purgative dose of magnesium sulphate. Dextrose and fluids freely, but *not* oils or fats. (Inhaled.) Keep patient warm. Artificial respiration. Respiratory stimulants.

Deaths after carbon tetrachloride have occurred in Jamaica, and thymol is now the drug of choice against hookworms.—B. M. Wilson, *Brit. med. J.*, ii/1928, 207. Carbon tetrachloride a proved potent liver poison and should not be given to a purged and fasting patient unless sufficient glucose is given at the same time.—H. M. Hanschell, *ibid*

Larger doses than 3 ml unnecessary and possibly dangerous. Wide variations in individual reaction to drug; 20 ml have been given. Alcoholics especially susceptible, 1.5 ml. having produced toxic symptoms in an acute alcoholic.—W. G. Smillie and S. B. Pessoa, per *J. trop. Med. (Hyg)*, i/1923, 127.

The livers of dogs receiving 3 ml. by the mouth were badly damaged. Since the danger is greatest during the first few minutes after reaching the duodenum, give a saline purge immediately.—H. S. Wells, *J. Pharmacol.*, 1925, 235.

Poisoning due to production of hypoglycæmia. Relieved by intravenous calcium therapy.—A. S. Minot, *ibid.*, 1931, 312.

Its use in hairdressing (for making the hair look clean and glossy) is reprehensible on account of the risks of serious poisoning. Two cases recorded.—*Brit. med. J. Ept.*, i/1933, 5

**Uses.** It has been extensively used in ankylostomiasis (*syn.* uncinariasis, dochmiasis, hookworm infection).

The vapour inhaled relieves hay fever. Employed locally, sprinkled on piline or lint covered with American oiled cloth, it quickly relieves neuralgic pains.

In Fiji 27,000 people treated without a casualty.—S. M. Lambert, per *J. trop. Med. (Hyg.)*, 1923, 92.

**Action on the liver.** Inadvisable to prescribe 5 ml doses as an anthelmintic with purgation, let alone without it. 3 ml., however, appears safe. It is specific for ankylostomes, and is fairly efficient for *ascaris lumbricoides* and *oxyuris vermicularis*, but of little value in the elimination of *trichuris trichiura*.—J. F. Docherty and E. Burgess, *Brit. med. J.*, ii/1922, 907.

Moderate alcoholism is not a contraindication, providing liquor is withheld two or three days before and after treatment. Saline purgatives should not be given immediately before treatment. The drug should never be given during the course of an infectious disease. In surgical cases where it is desired to rid patient of hookworm the drug should be given several days before the use of an anæsthetic.—C. N. Leach and co-workers, per *J. trop. Med. (Hyg)*, 1923, 47.

Pregnancy not a contraindication where *Necator americanus* is the offending agent.—*J. Amer. med. Ass.*, 1/1928, 736.

Follow with a saline purge. Unsuitable for weak individuals and those with liver derangement. Fats and alcohol should be avoided and a diet rich in carbohydrates and poor in fats is indicated. Can be given in kala-azar and malaria during remissions of fever, and is safe for pregnant women. Superior to chenopodium for necators and on a par in removing ankylostomes. With chenopodium has a distinct ascariocidal action and orally has more action on *oxyuris* than any other anthelmintic. Promising also by rectal injection in warm milk. Little action against *trichuris*, *strongyloides*, or tapeworms.—A. C. Chandler and A. K. Mukerji, *Indian med. Gaz.*, 1925, 68.

The addition of chenopodium of no value in pure necator infections, but the combination is more powerful on ankylostomes than either drug alone. A dosage of 60 m. of carbon tetrachloride in milk and 15 m. of oil of chenopodium in a capsule is safe for controlled patients.—A. C. Chandler and A. K. Mukerji, *Indian med. Gaz.*, 1925, 147. Combined almost ideal.—*Lancet*, 1/1930, 27.

More than 225,000 persons treated in Siam since May, 1923, with a mixture of oil of chenopodium (40%) and carbon tetrachloride (60%). Maximum dose 2 ml. Three deaths reported.—*Per J. Amer. med. Ass.*, 11/1925, 1001.

A dose of 3 to 4 ml for an adult of carbon tetrachloride is as safe or safer than any other anthelmintic, provided it is accompanied or followed by a saline purge, patient is well nourished and has normal liver, has adequate amount of calcium in his diet, refrains from use of alcohol before and after treatment, is given diet rich in carbohydrates and poor in fats, and is not starved preliminary to treatment, the drug being given about 3 hours after a moderately light carbohydrate and protein meal. Heavy ascariis infection a contraindication unless the drug is given in combination with oil of chenopodium. A single dose of 3 to 4 ml is safer than a smaller amount given in divided doses.—R. N. Chopra and A. C. Chandler, *Anthelmintics and their Uses* (Baillière, Tindall and Cox, 1928).

60,000 hookworm patients received treatment at the Old Cairo Hospital (C.M.S.) during 8 years. Writing October, 1928, the treatment most favoured was carbon tetrachloride and chenopodium oil, or thymol with magnesium sulphate intervening—course spread over 12 days.—Miss C. C. Byrd, *Brit. colon. Pharm.*, Oct., 1928.

A mixture of carbon tetrachloride 2 and chenopodium oil 1, given to children, 0.1 ml. for every year of age up to a maximum of 1.5 ml.—*Colon med Rep.*, No. 207, p. 33.

More than 100,000 consecutive treatments of hookworm disease without a death, and with few untoward symptoms.—S. M. Lambert, *J. Amer. med. Ass.*, 1/1933, 248.

Many hundreds of cases of hookworm treated as a routine measure every six months without complaints even of discomfort. The method of administration recommended is to give 3 ml. of carbon tetrachloride (Tetraform) in 15 ml. of castor oil (or liquid paraffin). No purgative is needed after its use.—A. S. Tuxford, *Lancet*, 1/1935, 1302.

A reurvey of hookworm disease in Fiji in 1935, 10 years after mass treatment with carbon tetrachloride, indicated that infection was only half of what it had been before the treatment campaign, and that infection was less severe in form. After 10 years there were still few clinical manifestations of hookworm disease in areas where formerly there had been almost universal anaemia.—S. M. Lambert, *J. trop. Med. (Hyg.)*, 1936, 21.

**DISTOMIASIS OF SHEEP.**—Carbon tetrachloride 1 ml. in capsule, without previous starvation is generally sufficient to clear adult flukes from the bile ducts. Some flocks tolerate the drug badly and it is best to try it on a few sheep first.—*Lancet*, 11/1927, 128.

Of value by the mouth and intravenously in human schistosomiasis and in distoma infestation of cattle.—F. G. Cawston, *Brit. med. J.*, 11/1928, 207. Usual single dose 2.5 to 3 ml.—F. G. Cawston, *Proc. R. Soc. Med.*, Nov., 1928, 245.

**Butolan** (Bayer Products, London) Carbaminic acid ester of *p*-oxydiphenylmethane. For oxyuriasis (thread-worm) Dose—1 or 2 tablets (7½ grains each) three times daily for one week.

**Dichlorethylene** (B.P.C.). *Syn.* ACETYLENE DICHLORIDE  $C_2H_2Cl_2$  = 96.93.

A heavy mobile liquid, with slightly acrid ethereal odour, consisting of a mixture of two stereoisomers boiling at 48° and 60°, and having sp. gr. of about 1.30. It is not readily inflammable and is suggested to replace ether for laboratory use. It is the best known solvent for rubber.

Is employed as a solvent of iodine for sterilising the skin. 2.5% w/v is used, i.e., practically a saturated solution. This solution is said to cause the operating surgeon or assistants no lachrymation or catarrh of the nasal mucous membrane which the methylated spirit tincture produces.

**Æthyleni Dichloridum** (B.P.C.). *Syn.* Dichlorethane  $C_2H_4Cl_2$  = 98.95. A mobile liquid with ethereal odour and sweet taste. B.p. 84°. Used as a solvent of iodine (1 in 40) for skin disinfection.

**Trichlorethylene.** *Prop. Names.* WESTROSOL (Imperial Chemical Industries, London), CHLORYLEN (Schering, London), TRILENE (Imperial Chemical Industries, London; Pharmaceutical Specialities (May & Baker) Ltd., London).

$\text{CHCl}_3 : \text{CCl}_4 = 131.4$ . Colourless liquid b.p.  $88^\circ$ , sp. gr. 1.47.

**Uses.** For trigeminal neuralgia 10 to 20 minims may be inhaled from cotton wool. Not more than 60 minims in twenty-four hours. Externally, an ointment, 1 in 4, in soft paraffin, destroys body lice, and soap solutions containing 2% may be used for cleaning the body. Used in commerce for the solution of tarry, bituminous products, rubber, sulphur, phosphorus, and for dry cleaning.

A powerful "degreaser," and as a wound cleanser greatly superior to surgical spirit, methylated spirit, etc. It is also a good solvent for tar and is particularly useful in the treatment of tar burns. A boy of 9 playing with a tar-spraying machine received very extensive burns, following cleansing with trichlorethylene and coagulation with Tannaflavine he made an uninterrupted recovery—H. B. Trumper, *Brit med J*, ii/1934, 1219.

Dangers from its growing popularity as a cleansing agent. Three cases of acute, but not fatal, poisoning in a factory. In 1931, in Germany, 284 cases of poisoning were recorded by Stuber, including 25 deaths—*Per Brit med J Ept*, i/1934, 21.

**ANGINA PECTORIS.**—Inhalation of 1 ml. morning and evening relieved the distress and apprehension in most cases.—J. C. Krantz, *J. Amer med Ass.*, i/1936, 485.

**TRIGEMINAL NEURALGIA.**—Cases treated with trichlorethylene, symptoms relieved.—M. A. Glaser, *J. Amer. med Ass*, i/1931, 920.

**Trichlorethylene Sterules** (*Martindale, London*) Ampoules containing 10 m. and encased in cotton wool and silk, to be broken between the fingers and the vapour inhaled.

**Tetrachlorethyleneum (B.P.C.)** *Syn* PERCHLOR-ETHYLENE.  $\text{C}_2\text{Cl}_4 = 165.8$ .

**Dose.**—15 minims (1 ml) in capsules. For ankylostomiasis doses totalling 3, 4 and 5 ml. are given at hourly intervals on each of three consecutive days; on the third day, 3 hours after the last dose, give saline purge.

Colourless heavy mobile liquid with odour similar to that of carbon tetrachloride B.p.  $117^\circ$  to  $122^\circ$ ; sp. gr. about 1.62. Insoluble in water; miscible with alcohol 90%, ether and oils. Used for the expulsion of hookworm in man and animals and of roundworms in animals.

**ANKYLOSTOMIASIS.**—An extremely valuable substance for the treatment of uncomplicated hookworm disease. Thought to be as effective against hookworm as carbon tetrachloride, but should not be classed with the latter as a toxic anthelmintic. Ineffective against ascaris.—P. D. Lamson and co-workers, *J. Amer med. Ass.*, ii/1932, 293.

Much less toxic in cats than carbon tetrachloride and harmless in therapeutic doses. A mixture of 2 ounces of saturated magnesium sulphate with 4 ml of tetrachlorethylene and 1 ml of oil of chenopodium, shaken to form a fine emulsion and given immediately, gave 62% of cures with one treatment in 50 cases.—P. A. Mapleston, A. K. Mukerji and R. N. Chopra, *Indian med. Gaz.*, 1933, 554 and 617.

More than 46,000 treatments of hookworm disease without a death, and with few untoward symptoms. The most satisfactory anthelmintic so far developed for hookworm disease.—S. M. Lambert, *J. Amer. med. Ass.*, i/1933, 248.

Tetrachlorethylene is a safe and reliable anthelmintic for general use when properly administered. Potency increased by addition of oil of chenopodium.—D. Manson, *Indian med. Gaz*, 1934, 500.

**Chlorine Derivatives of Methane, Ethane and Ethylene** increase in toxicity with increase in number of Cl atoms.—G. S. Barsoung and K. Sead, *Quart. J. Pharm.*, 1934, 192.

**Tetrachlorethane.** *Syn. and Prop. Name.* ACETYLENE TETRACHLORIDE, WESTRON (*Imperial Chemical Industries, London*)

$C_2H_2Cl_4 = 167.8$ .

A liquid with penetrating odour, b.p. about  $146^\circ$ ; sp. gr. about 1.6. It dissolves oils, fats, waxes, and resins, and sulphur (1% at ordinary temperature), phosphorus and chlorine.

Used as a solvent for varnishes, especially cellulose acetate, and as a paint-remover and degreaser. Extensively employed as an insecticide, especially for white fly on tomato plants and for weevils 10 fl. oz. being allowed to volatilise for 1000 cu. ft.

**Pentachlorethane,**  $C_2HCl_5 = 202.3$ , is similar. B.p.  $159^\circ$

**Hexachlorethane.**  $C_2Cl_6 = 236.7$

A solid subliming at  $185^\circ$  without melting almost insoluble in water, more soluble in alcohol and ether, or a mixture of the two. It has a smell similar to camphor, for which it is used as a substitute in the celluloid industry. Also employed to render substances non-inflammable in explosives industry, and is incorporated in anti-fouling paints.

**Cyclohexanol.**  $C_6H_{11}OH$  *Prop. Name.* SEXTOL (*Howard & Sons, Ilford*). Is prepared by the catalytic hydrogenation of phenol, using nickel at about  $180^\circ$ . It is a solvent for fats, waxes, resins, rubber, celluloid, etc., but is principally used in conjunction with soaps—with which it forms clear aqueous solutions—as a detergent, in laundry and textile work.

Its derivatives, cyclohexanyl acetate (Sextate) and cyclohexanone (Sextone), and also the methylcyclohexanols (methylhexalin), produced by hydrogenation of the mixed cresols, are similarly employed.

## CARYOPHYLLUM

(with CARDAMOMUM, etc.)

B.P., U.S.P. XI, P. Dan.

*Dose* — 2 to 5 grains (0.12 to 0.3 g.).

The dried flower-buds of *Eugenia aromatica* (Myrtaceæ).

In senile flatulence good effects are produced by powdered cloves, better even than a fluid preparation. Spirit of cloves is absorbed in the stomach but the woody fibre passes on to the seat of the complaint.

**Aqua Caryophylli Destillata** (B.P.C.) *Dose* —  $\frac{1}{4}$  to 1 ounce (15 to 30 ml.). 1 in 40.

**Aqua Caryophylli Concentrata** (B.P.C.) *Dose* — 5 to 15 minims (0.3 to 1 ml.). Contains 2% v/v of oil of clove and is approximately 40 times the strength of the distilled water.

**Aqua Mellis** (B.P.C.) HONEY WATER

Oils of bergamot, lavender, clove and sandal wood, musk and saffron with triple rose water, triple orange-flower water, honey and alcohol 90%

**Infusum Caryophylli Concentratum** (B.P.) *Dose* —  $\frac{1}{4}$  to 1 drachm (2 to 4 ml.). 1 in 5.

**Infusum Caryophylli Recens** (B.P.) *Dose* —  $\frac{1}{4}$  to 1 ounce (15 to 30 ml.). 1 in 40.

**Tinctura Caryophylli.** 1 in 8 of alcohol 90%. Digest 10 days *Dose* — 20 to 40 minims or more: aromatic, carminative and stimulant

**Oleum Caryophylli** (B.P., U.S.P. XI, P. Helv. V).

*Dose.* — 1 to 3 minims (0.06 to 0.2 ml.).

Colourless to brownish oil. Contains 85 to 90% v/v of eugenol,  $C_{10}H_{18}O_2$ . Soluble 1 in 2 of alcohol 70% (80% P. Ital. V).



**Aromatic carminative.** Given with advantage both internally, 3 to 5 minims, and injected hypodermically in phthisis, 5 minims in olive oil. A satisfactory disinfectant for the hands (said to be even more efficient than mercuric chloride), catheters, catgut, etc.

**Eugenol** (*B.P.C., U.S.P. XI, P. Dan.*). *Syn.* EUGENIC ACID, 2-Methoxy-4-allylphenol.  $C_6H_5(OH)(OCH_3)C_3H_5$ , 4 : 3 : 1 = 164.1.

*Dose.*—1 to 3 minims (0.06 to 0.2 ml.).

A colourless oily liquid, b.p.  $251^{\circ}$  to  $253^{\circ}$ ; *U.S.P. XI*  $250^{\circ}$  to  $255^{\circ}$ ; darkening on exposure. It is the chief constituent of oil of clove and has a strong clove odour. Is a powerful antiseptic and antiputrescent. Is employed by dentists as an abundant causing reduced sensibility of mucous membrane, but not complete anaesthesia. Useful with wool fat in eczema.

**Isoeugenol**, used in perfumery for its carnation-clove odour and for the manufacture of vanillin, is obtained by heating eugenol with potassium hydroxide.

**Cardamomum** (*B.P., U.S.P. XI, P. Helv. V*). *Syn.* CARDAMOMI SEMINA, FRUCTUS CARDAMOMI (*P. Dan.*).

The dried ripe seeds of *Elettaria Cardamomum* var. *minuscule* (*Zingiberaceae*). The seeds should not be removed from their fruits until required for use. Given in atonic dyspepsia. Contained in Pulvis Aromaticus.

**Tinctura Cardamomi Aromatica** (*B.P.C.*) *Syn.* TINCTURA CARMINATIVA. *Dose.*—2 to 10 minims (0.12 to 0.6 ml.).

Cardamom about 1 in 16 with strong tincture of ginger and oils of caraway, cinnamon and clove.

**Tinctura Cardamomi Composita** (*B.P.*).

*Dose.*— $\frac{1}{2}$  to 1 drachm (2 to 4 ml.). Cardamom 1.4% with caraway, cinnamon, cochineal, glycerin and alcohol 60%. Is more or less decolorised by alkaloidal salts, bismuth oxide, oxycarbonate and subnitrate employ Liquor Bismuthi in preference. Also by metals of the alkaline earths and sodium bromide.

Colour of compound tincture of cardamom depends on change of pH; buffer salt added—to give a constant pH of 7—stabilises. There should be no contact with iron or copper in percolation.—R. R. Bennett and G. Middleton, *Pharm. J.*, ii/1926, 173.

**Tinctura Cardamomi Composita** (*U.S.P. XI*).

*Average dose.*—60 minims (4 ml.).

Cardamom seed 2, cinnamon 2.5, caraway 1.2, cochineal 0.5, glycerin 5, in diluted alcohol to 100.

**Oleum Cardamomi** (*B.P.C.*). *Dose.*— $\frac{1}{2}$  to 3 minims (0.03 to 0.2 ml.).

Obtained from the whole fruits of cardamom. Aromatic carminative.

**Carum** (*B.P., U.S.P. XI*). *Syn.* CARUI FRUCTUS, CARAWAY FRUIT or SEED.

*Dose.*—10 to 30 grains (0.6 to 2 g.). The dried ripe fruits of *Carum Carvi* (*Umbelliferae*).

**Aqua Carui Destillata** (*B.P.C.*). *Syn.* AQUA CARUI DESTILLATA. *Dose.*— $\frac{1}{2}$  to 1 ounce (15 to 30 ml.). 1 in 10.

**Aqua Carui Concentrata** (*B.P.C.*). *Dose.*—5 to 15 minims (0.3 to 1 ml.). Contains 2% v/v of oil of caraway and is approximately 40 times the strength of the distilled water.

**Oleum Carui** (*B.P., P. Helv. V*). *Syn.* OLEUM CARUI.

*Dose.*—1 to 3 minims (0.06 to 0.2 ml.).

Contains 53 to 63% w/w of carvone,  $C_{10}H_{14}O$ . Soluble 1 in 1 of alcohol 90% and 1 in 7 of alcohol 80%.

Carvone,  $C_{10}H_{14}O$ , the principal constituent of oil of caraway, occurs also in oils of dill and spearmint. It is a colourless or slightly yellow liquid, miscible with alcohol.

**Coriandrum** (*B.P., P. Dan.*).

*Dose.*—5 to 15 grains (0.3 to 1 g.).

Dried ripe fruits of *Coriandrum sativum* (Umbelliferae). Aromatic and carminative.

**Oleum Coriandri** (B.P.). *Dose*.—1 to 3 minims (0.06 to 0.2 ml.). Is added to preparations of rhubarb and senna to prevent griping.

**Myrica** (B.P.C.). *Dose*.—10 to 60 grains (0.6 to 4 g.).

The dried root-bark of *Myrica cerifera* (Myricaceae). Tonic and astringent, emetic in large doses. Is an ingredient, together with various proportions of ginger, capsicum and clove, of COMPOSITION POWDER or COMPOSITION ESSENCE used as a domestic remedy for colds.

**Myricin**. *Dose*.—2 to 5 grains. The powdered extract of *Myrica cerifera*. An astringent and stimulant, and in large doses, emetic. For diarrhoea and jaundice.

**Myristica** (B.P., U.S.P. XI, P. Helv. V). SYN. NUX MOSCHATA, NUTMEG.

*Dose*.—5 to 10 grains (0.3 to 0.6 g.). The dried kernels of the seeds of *Myristica fragrans* (Myristicaceae).

**Oleum Myristicæ** (B.P., U.S.P. XI). *Dose*.—1 to 3 minims (0.06 to 0.2 ml.). Distilled from nutmeg. Soluble 1 in 3 of alcohol 90%.

**Oleum Myristicæ Expressum**. SYN. ADEPS MYRISTICÆ, MACE BUTTER. Bright orange, solid fat obtained from nutmeg or mace by hot expression. Is a mild stimulant and has been incorporated in plasters.

The expressed or concrete oil of nutmeg of yellowish colour contains myristicin,  $C_{15}H_{11}O_2 = 206$ . It is occasionally employed as a gentle local stimulant. It is stated to have narcotic properties.

**Spiritus Myristicæ** (B.P.C.). *Dose*.—5 to 20 minims (0.3 to 1.2 ml.) 1 in 10.

**Oleum Myristicæ Deterpenatum** (B.P.C.). Terpenless Oil of Nutmeg. Is prepared by concentration *in vacuo* and is about 5 times as strong as oil of nutmeg.

**Oleum Myrciæ** (B.P.C.). OIL OF BAY.

Is obtained from *Pimenta acris* and other species. Occurs as a yellow liquid becoming brown on exposure to air. Soluble when fresh in an equal volume of alcohol 95%, less soluble on keeping.

**Spiritus Myrciæ Compositus** (B.P.C.). SYN. SPIRITUS PIMENTÆ COMPOSITUS.

Contains oils of bay, orange and pimento, and dry extract of quassia in diluted alcohol. Preparations of similar composition and coloured brown are sold as bay rum.

**Pimenta** (B.P.C.). SYN. PIMENTO, ALLSPICE, JAMAICA PEPPER.

The dried full-grown unripe fruits of *Pimenta officinalis* (Myrtaceae).

**Aqua Pimentæ Concentrata** (B.P.C.). *Dose*.—5 to 15 minims (0.3 to 1 ml.). Oil of pimento 1 in 50. This preparation diluted 1 to 40 with water is to be dispensed for Aqua Pimentæ.

**Oleum Pimentæ** (B.P.C.).

*Dose*.— $\frac{1}{2}$  to 3 minims (0.06 to 0.2 ml.).

Soluble 1 in 3 of alcohol 70%, miscible with alcohol 90%. Eugenol content not less than 80% v/v. Stomachic and antispasmodic.

## CASCARA SAGRADA

B.P., U.S.P. XI, P.G. V, P. Ital. V, F.E. VIII, P. Helv. V, P. Belg. IV.

SYN. SACRED BARK.

*Dose*.—20 to 60 grains (1.2 to 4 g.) in cachets.

The dried bark of *Rhamnus Purshiana* (Rhamnaceæ).

The active constituents of cascara cannot be defined. *B.P.* and *U.S.P. XI* require the bark to be kept at least one year. The tree grows extensively in British Columbia.

*P. Ital. V* requires the bark to yield not less than 24% extractive and not more than 6% ash.

**Uses.** Increases peristalsis, empties rectum, it is useful for internal piles, and is a good laxative. For dosage see Liquid Extract.

### **Elixir Cascaræ Sagradæ (B.P.).**

**Dose.**—30 to 60 minims (2 to 4 ml.).

1 in 1, prepared by percolating with boiling water a mixture of cascara, liquorice and light magnesium oxide, evaporating, and adding alcohol, glycerin and flavouring agents. It is practically free from bitterness but is sometimes alleged to be less active therapeutically than the liquid extract.

### **Fluidextractum Cascaræ Sagradæ Aromaticum (U.S.P. XI)**

**Average dose.**—30 minims (2 ml.)

Closely resembles the elixir of the *B.P.* 1932, but contains 0.01% of methyl salicylate and larger proportions of saccharin, oil of anise and alcohol.

*P. Ital. V* has also an aromatic liquid extract employing magnesia, with liquorice, glycerin, saccharin and anise.

### **Extractum Cascaræ Sagradæ Liquidum (B.P.).**

**Dose.**—30 to 60 minims (2 to 4 ml.).

An aqueous extract containing 25% of alcohol (90%). It may be made miscible with water by adding half its volume of sal volatile.

*P. Ital. V* is very similar. *P. Belg. IV* uses 60% alcohol. *P. Jap.* makes with alcohol 90% and water equal parts. *Fr. Cx. Supp.* 1926, with alcohol 50%, 1 = 1 by weight using 8% of light calcined magnesia in the extraction.

**Use in Constipation.** The initial dose depends on the individual, but it must be correctly found—15 to 20 drops *t.d.*, suffices for the adult. The object is to procure one motion only each day. The dose that is sufficient must be taken in a wineglassful of water thrice daily after meals for a week or ten days, or until the action becomes somewhat too pronounced. Then reduce dose by one drop only and take with the same regularity as before. In time it will be found that 1 drop in water thrice daily after meals will be sufficient. Finally the medicine may be omitted altogether.

After laparotomy, suitable aperients are confection of senna or the following: Ext. Cascaræ Sagradæ Liq. 1 oz., sodium sulphate 1 oz., solution of ammonia 40 m., chloroform water to 8 oz. **Dose.**—2 to 4 drachms night and morning—*C. W. Gordon Bryan, Lancet*, 11/1930, 1141.

### **Fluidextractum Cascaræ Sagradæ (U.S.P. XI).**

**Average dose.**—15 minims (1 ml.).

One ml. represents 1 g. of the bark; it is of the same strength as the liquid extract of the *B.P.*

### **Extractum Cascaræ Sagradæ Siccum (B.P.).**

**Dose.**—2 to 8 grains (0.12 to 0.5 g.) in pill.—An aqueous extract evaporated under reduced pressure, so as to produce a spongy mass which is readily granulated. *Fr. Cx.* and *P. Ital. V* extract with 60% alcohol.

**Extractum Cascaræ Sagradæ (U.S.P. XI).** **Average dose.**— $\frac{1}{2}$  grain (0.015 g.). 1 g. represents 3 g. of the bark.

**Mistura Cascaræ (Gt. Orm. H.).** (For 1 year old child.)

Liquid extract of cascara, liquid extract of liquorice, syrup of orange, chloroform water, of each 15 minims for one dose.

[P1] **Mistura Cascaræ Compositæ (B.P.C.).**

*Dose.*— $\frac{1}{2}$  to 1 ounce (15 to 30 ml.).

Contains 20 m. of liquid extract of cascara per ounce, with tincture of belladonna and tincture of nux vomica.

[P1] **Mistura Cascaræ Composita (L.H.).** *Syn.* MISTURA APERIENS (L.H.).

Liquid extract of cascara sagrada 1 dr, liquid extract of senna 30 m, liquid extract of liquorice 60 m., tincture of hyoscyamus 30 m, tincture of nux vomica 10 m., emulsion of chloroform 10 m., compound decoction of aloes to 1 oz

[P1] **Mist Cascar. c. Nuc. Vomica (N.I.F.).**

Liquid extract of cascara sagrada 20 m, ammonium carbonate 2 gr, tincture of nux vomica 5 m, tincture of belladonna 3 m, liquid extract of liquorice 20 m, chloroform water to  $\frac{1}{2}$  oz.

**Mistura Hepatica.** *Dose.*—1 to 2 drachms in water. Liquid extract of cascara 20, tincture of jalap 20, tincture of podophyllum 10, compound tincture of gentian 10, chloroform water 50, sal volatile 10

**P1 81] Pilulæ Cascaræ Compositæ (B.P.C.),** *dose* —1 to 3 pills, contain  $\frac{1}{2}$  gr. of dry extract of cascara with dry extracts of belladonna and nux vomica.

An agreeable and efficient aperient, with gentle action continuing beyond the first day; good for liver inaction.

**Syrupus Cascaræ Aromaticus (B.P.C.).**

*Dose.*— $\frac{1}{2}$  to 2 drachms (2 to 8 ml.) as laxative.

Contains 40% *v/v* of liquid extract of cascara flavoured with orange and cinnamon.

**Tabellæ Cascaræ Sagraæ (B.P.C.)** contain 2 gr. (0.12 g) of the dry extract.

**Tinctura Cascaræ Sagraæ.**

*Laxative Dose* —10 to 60 minims (0.6 to 4 ml.).

Percolate 1 to 5 with alcohol 60%.

[P1] **Tinctura Laxativa.**

*Dose.*—20 to 60 minims (1.2 to 4 ml)

Liquid extract of cascara sagrada 2, aromatic spirit of ammonia 2, spirit of chloroform 2, tincture of belladonna 1, tincture of nux vomica 1 This is an agreeable and elegant form of administering cascara, being miscible with water

**Trochisci Cascaræ Sagraæ et Olei Menthæ Piperitæ.**

These are made with fruit basis, and contain  $2\frac{1}{2}$  gr of extract flavoured with peppermint; they are useful correctives *Dose* —1 or 2

**Vinum Cascaræ.**

*Dose.*— $\frac{1}{2}$  to 1 ounce (15 to 30 ml.).

Liquid extract of cascara 1, sugar 1, aromatic elixir 1, sherry-type wine to 20 Mix and decant from any sediment which may form on standing

**Bitter-free Cascara (Martindale, London).**

*Dose.*— $\frac{1}{2}$  to  $\frac{1}{4}$  drachm increased.

A preparation to supply the tonic laxative properties of the bark while omitting the griping substances It is not made by means of magnesia.

**Cascagar (Martindale, London)**

*Dose.*—1 teaspoonful up to 2 tablespoonfuls to be taken with stewed apple or other moist food.

A preparation of flaked agar 90, with liquid extract of cascara sagrada 10, flavoured with lemon, also with raspberry, acting similarly to the preceding.

**Cascara Evacuant (Parke, Davis, London)** Palatable cascara preparation. *Dose.*—10 to 30 minims

[P1 81] **Hepatagen (Hewlett, London)** Contains extract of cascara, extract of rhubarb, jalapin, podophylin, cocaine hydrochloride, aromatics, etc.

*Dose.*—10 to 60 minims. In biliousness, hepatitis and chronic gastritis

**Kasak (Squire & Sons, London).** *Dose* for children, 1 or 2 drachms; adults,  $\frac{1}{2}$  ounce. A laxative free from bitterness.

**Kasena** (*Squire & Sons, London*). Similar to Kasak but contains senna.

**Kasena Capsules** are also made.

**Molevac** (*Parke, Davis, London*). Liquid paraffin, malt extract and Cascara Evacuant. *Dose*.—From one teaspoonful. Chronic constipation.

**Peristaltin** (*Ciba, London*). Natural glycosides of cascara sagrada. Supplied in tablets containing  $1\frac{1}{2}$  gr. and ampoules of 15 ml. (=  $2\frac{1}{2}$  gr.). *Dose*.—1 to 3 tablets daily or 1 or 2 ampoules daily hypodermically. In chronic constipation and post-operative intestinal paresis.

**Dihydroxyanthraquinone**. *Syn. and Prop. Name*. DIOXYANTHRACHINONUM (P.G. VI); *ISTIN* (*Bayer Products, London*) is dihydroxyanthraquinone in 0.15 g. tablets.  $\text{HO}\cdot\text{C}_6\text{H}_3\cdot\text{CO}\cdot\text{CO}\cdot\text{C}_6\text{H}_3\cdot\text{OH} = 242.1$ .

*Dose*.—2 to 6 grains (0.12 to 0.4 g.).

Orange crystalline powder, slightly soluble in water. *M p*  $190^\circ$  to  $192^\circ$ . A synthetic purgative.

**Isacen** (*Hoffmann-La Roche, London*) is DIACETYL-DIHYDROXYPHENYL-ISATINE, a synthetic purgative, which in small doses stimulates peristalsis by action upon the mucous lining of the colon and large intestine. It passes through the stomach unchanged and has no action upon the kidneys.

*Dose*.—2 to 4 granules, each  $\frac{1}{12}$  grain (0.005 g.).

**Frangula** (*B.P.C., P. Helv. V, P. Dan.*). *Syn.* ALDER BUCKTHORN BARK

The stem and branches of *Rhamnus Frangula* (Rhamnaceæ). Indigenous to Europe and America. Should be one year old. Cathartic especially for hæmorrhoids and chronic constipation, resembles cascara in constituents and action. Liquid Extract *B.P.* '85 (1 = 1). *Dose*.—1 to 4 drachms.

**Rhamnus** (*B.P.C.*). *Syn.* BUCKTHORN.

The fresh ripe fruit of *R. cathartica* (Rhamnaceæ).

**Syrupus Rhamni** (*B.P.C.*). *Dose*.— $\frac{1}{2}$  to 1 drachm (2 to 4 ml.). A solution of sucrose in the juice expressed from buckthorn, with oil of pimento. A laxative, used chiefly in veterinary practice.

**Normacol** (*Norgine, Prague; Napp, London*)

*Dose*.—1 to 2 drachms in a glass of water once or twice daily

A preparation of dried plant mucilage of the bassorin type containing a little buckthorn extract. For treatment of habitual constipation

Bassorin is the name given to the insoluble portion of many gums—karaya, tragacanth, etc. It swells up with water, but is not soluble.

**Juglandin**. An extractive prepared from the inner bark of the root of *Juglans cinerea*, the North-American butter nut, is an hepatic stimulant and cathartic. *Dose*.—2 to 5 grains in pill. **Spiritus Nucis Juglandis**, distilled from *Juglans regia*, the common European walnut, is an antispasmodic and has been used for checking sickness of pregnancy. *Dose*.—1 to 4 drachms. **Folia Juglandis** are in *P. Austr.*; also in *P. Belg.* (and Fluid Extract) and *P. Helv. V.*

## CASEINUM

**Casein** is the principal albuminoid constituent of milk, and is present in solution in the aqueous portion of the milk as an alkali-albuminate, probably as a calcium compound (the alkali in milk is about 0.5%). Some hold that casein exists as caseinogen, and that this is converted into casein by ferment. It is precipitated by dilute acids and by the enzyme, rennet. Casein is present in milk to the extent of 3 to 5% (usually about  $3\frac{1}{2}\%$ ). Once thrown out of solution it is not readily dissolved again except with added alkali or hydrochloric acid. Cheese is casein with a considerable proportion of fat.

**Caseinum Solubile** (*B.P.C.*).

A compound of casein with a small proportion of alkali which renders it almost entirely *soluble* in water.

**SYNTHETIC MILK.** For use when milk is forbidden, as in a strictly salt-free diet, has been prepared from water, lactose, cream, "ashless" casein ("a special acid-washed first grade acid casein"), and a salt mixture containing calcium, magnesium, potassium, iron and phosphorus. A salt-free bread containing 19.7% of protein may also be prepared, using "ashless" casein.—E. M. Widdowson and R. A. McCance, *Lancet*, 1/1935, 1437.

**Pigmentum Casein.** *Syn.* UNGUENTUM CASEINÆ. Casein 14, potassium carbonate  $\frac{1}{2}$ , glycerin 7, soft paraffin 21, zinc oxide  $\frac{1}{2}$ , phenol  $\frac{1}{2}$ , water to 100. If good casein be used this is almost too thick—add a little more water. A basis for skin medicaments. Thymol *q.s.* may be added to preserve it.

**Fissan Brand Products** (*Genatosan, Loughborough*). A series of preparations including dusting powders, ointments, etc., whose base is an "albumin colloid isolated from milk," which is rendered especially effective by means of a light powder, "fluoro-silica colloid."

### Notes on Artificial Feeding with Cows' Milk and Casein Products.

**Human milk** has the average composition:—Fat 3.4%, lactose 6.4%, albuminoids 1.7% (casein and lactalbumen), mineral matter 0.2%. (The difference between human milk and cows' milk in the relationship between the albuminoids and the mineral matter is dealt with in *Vol. II*.)

If artificial feeding has to be resorted to, Tuberculin Tested cows' milk (*see Vol. II*) should first be tried, as a general rule diluted with an equal quantity of water. Milk sugar, a drachm to the pint, is also a useful addition. The product contains approximately the same proportion of protein as human milk but is low in fat and sugar.

**Artificial human milk** may be made from diluted milk by addition of cream, or other fat, and lactose. To 4 oz. of diluted milk add 1 teaspoonful of lactose and 1 teaspoonful of cream (Hutchison & Mottram, *Food and Principles of Dietetics*). Instead of adding cream, "upper milk" may be used instead of whole milk. This consists of the upper portion of milk that has stood in a cool place until a cream layer has formed. By diluting with water, or with water and whole milk, mixtures are obtained containing a high percentage of fat with a normal percentage of protein. Upper milks are much superior to cream mixtures for feeding—the fat percentages are more uniform and the dilutions do not so readily separate as those employing cream.

Sodium citrate, 1 gr. per oz., may be added to prevent clotting in the stomach.

Alternatively, the extra fat may be incorporated in the form of Emulsio Olei Arachis, *B.P.C.*

**New Zealand Cream** (*Mothercraft Training Society, London*), an emulsion of 50% fats and oils (3 parts of animal oil, 1 part of vegetable oil, mainly arachis oil) with 40% of sugars (dextrose and a little lactose), is used for the same purpose.

If the above is not digested, partially peptonised milk must be given, employing peptonising powders or Liquor Pancreatini *q.v.*

**Cows' Milk, Modification to Breast Standard.** The following formula is given:—Milk (of average quality) 10 oz., cream (33%) 1 oz. (or cream 48%,  $\frac{1}{2}$  oz.), sugar (lactose at first, but

later lactose, maltose and cane sugar mixed) 1 oz., broth 4 oz., water to 1 pint. The addition of broth has been found good—E. Pritchard, *Lancet*, 1/1922, 838.

**Dried Milks** are prepared either by spraying milk in a current of hot air, or by heating over revolving cylinders.

Dried milk made by the roller process rarely has bacterial content of more than 1000 per gramme. The total bacterial count and the total count of hæmolyzing colonies much higher in milk prepared by spray process than by roller process.—E. M. Bexby, *J. Amer. med. Ass.*, 11/1929, 150.

Milk dried by the roller process has a greater amount of antiscorbutic vitamin than spray-process milk.—E. Mellanby, *Brit. med. J.*, 1/1924, 895.

For infant feeding, the "half-cream" milk is preferred by some authorities, as being less rich. This contains perhaps only 1% fat. *B. tuberculosis* is killed in the process of desiccation. For infant feeding and general use are:—

**Dried Full-Cream Milk** is reconverted into milk by mixing 2½ oz. (5 heaped tablespoonfuls) with 1 pint of hot water.

**Dried Half-Cream Milk.** Employ 2½ oz. (5 tablespoonfuls) to the pint of hot water.

**Dried Separated Milk** (containing 1% of its original butter-fat). Employ 2 oz (4 heaped tablespoonfuls) to the pint of hot water.

Dried milk is more easy of digestion. Infants are often unable to take fresh milk even in extreme dilution without recurrence of diarrhœa, yet can digest comparatively concentrated mixtures of dried milk. Get the child back again on cows' milk gradually. A teaspoonful or less to be added to the dried milk at first and increased.

(For particulars of the composition of cows' and other milks, also of condensed milk, graded milks, and of the effects of pasteurisation, see Vol. II.)

**Whey Powder.** This is desiccated milk deprived of fat and casein. It has average composition:—Soluble lactalbumen 14.25, lactose 74.45, fats 0.27, mineral matter, chiefly phosphate, 9.8, moisture 1.2%. It is employed in conjunction with cows' milk for producing a milk with a reduced proportion of casein, and also of higher sp. gr., with the result that the amount of fluid is proportionally lessened. Or it may be prepared with water and cream—the cream being low in casein, sugar and ash, but high in fat, whilst the whey is low in fat, but high in ash, sugar and lactalbumen. It may also be used alone to produce milk whey by dissolving in water.

Human milk contains on an average 0.8% of casein and 0.6% of lactalbumen; cows' milk 2.7 to 3% of casein and 0.2 to 0.3% of lactalbumen. (For other constituents see Vol. II.) In diluting cows' milk with water to reduce the casein content it is obvious that the deficiency in lactalbumen is rendered still more in error.

It is also clear, if the preceding figures be correct, that a breast-fed child taking 1000 g. of milk in a day will receive 6 g. of

**lactalbumen.** *A child receiving, say, 600 g. of cows' milk would receive only 1.8 g., at most, of the same albumen. This lactalbumen is soluble, i.e., it does not undergo precipitation with acid and digestion with pepsin and pancreatin before assimilation.*

Arguing by analogy with the high albumen content in colostrum which the newly-born calf receives, the advocates of lactalbumen as an addition to cows' milk for infants' milk, claim that it is important to supply the infant with a form of protein which makes small demand on the digestive glands, and which does not require much transformation before it can be absorbed.

**Koumiss (Artificial).** Dissolve dextrose  $\frac{1}{2}$  ounce in water 4 ounces, and add 20 grains of yeast and cows' milk 4 ounces. Place in a quart bottle and fill up with milk; cork and wire. Keep it cool and shake it frequently during 4 days. Koumiss thus prepared contains some alcohol (1 to 2%) and lactic acid (about 1 to 2%). The original koumiss of the Tartars was made from mares' milk by using the peculiar Kephir ferment, which swells up on soaking in milk. This consisted in reality of yeast cells with certain bacteria (*B. Caucasicus*, Kern). It is a food used in the Caucasus as a stimulant in exhaustion and in convalescence of phthisis. Was recommended by Metchnikoff as a nutritive and as an intestinal antiseptic. See also *Acid Lactic Bacilli*, this Vol and Vol II.

## PROPRIETARY FOODS

**Allenburys Foods** (*Allen & Hanburys, London*) No. 1 (for infants up to 3 months old) consists of dried milk from which excess of caseinogen has been removed and vegetable protein, lactose, and milk fat added, together with dextrin-maltose and vitamin D. No. 2 (for infants from 3 to 6 months old) is similar, but contains malted flour, free from starch. No. 3 (for infants more than 6 months old) consists of partially baked wheat flour with malt. A half-cream food and a food with additional iron are also available.

**Almata** (*Keen, Robinson, Norwich*) It is made from egg-yolk, butter-fat, dextrin-maltose, and decitrated fresh fruit juice and contains the needed mineral constituents. It is also of value as a galactagogue and an invalid food.

**Ambrosia** (*Ambrosia, London*) A dried milk powder. Also available humanised.

**Benger's Food** (*Benger's Food, Manchester*). A wheaten flour preparation containing trypsin and amylase. It is used with fresh milk or milk and water. It gives nourishment with complete or partial rest to the digestive system. The point of the preparation is that if the digestive system, however weak, can do any work at all, it should be given it to do to the extent of its power. The fat may be increased by adding cream or upper-milk.

**Brestol** (*Cow & Gate, Guldford*) "Humanised cream" with cod-liver oil and concentrated orange juice. As substitute for dairy cream and cod-liver oil emulsions in cases of fat intolerance and in backward and underweight babies, also in marasmus and tuberculosis.

**Casec** (*Mead, Johnson & Co., Evansville, U.S.A.; Brooks & Warburton, London*) Calcium caseinate, to correct diarrhoea and other nutritional disturbances of infants.

**Casumen** (*Prideaux, London*). A soluble form of casein (Flocculent Casein) containing a very high percentage of protein (90%). For use in all cases of poor nutrition. It contains practically no fat or sugar. It may be mixed with cocoa, chocolate, bread (10%) for diabetics, etc.

**Colact** (*Glaxo Laboratories, London*) Beverage of milk solids, cocoa and sugar with a concentrate of vitamins A and D. Each cupful made as directed contains vitamins A and D equivalent to 1 pint of best summer milk.



**Cow & Gate Milk** (*Cow & Gate, Guildford*) Dried milk without added sugar.

**Energen Bread** (*Energen Foods, London*). Contains 40% of protein and only 46% of starch. Its caloric value is 108 cal. per oz. (ordinary bread 75 cal. = 1 oz.). Energen Bread and Breakfast Food (Bisméal) are rich in protein and much reduced in starch, and are of value in cases requiring strict dietary.

**Farex** (*Glaxo Laboratories, London*). A preparation of wheat flour, wheat germ, oatmeal, cornmeal, edible bone meal, yeast and a concentrate of vitamins and minerals (including calcium, phosphorus, iron, copper and vitamins A, B<sub>1</sub>, B<sub>2</sub> and D). It does not require cooking. An invalid diet and in the treatment of gastro-intestinal disorders.

**Ferrolac** (*Glaxo Laboratories, London*). Full-cream milk food, each pound containing 31½ gr. of iron and ammonium citrate, yielding 125 p.p.m. of iron when reconstituted, also vitamin D 165 i.u. per pint

**Frailac** (*Cow & Gate, Guildford*). A reconstituted milk specially devised for frail and premature babies.

**Glaxo, Full-Cream** (*Glaxo Laboratories, London*). Resembles Sunshine Glaxo, but retains full fat and protein content of cows' milk, and contains, when reconstituted, 165 i.u. of vitamin D per pint and 5 p.p.m. of iron. For infants after first 3 or 4 months.

**Sunshine Glaxo** is adjusted to a "humanised" formula and contains when reconstituted, 200 i.u. of added vitamin D (Calciferol) per pint and 5 p.p.m. of iron. Specially suited for infants in first 3 or 4 months of life

**Glax-Ovo** (*Glaxo Laboratories, London*). Described as a tonic malted food beverage. A palatable, readily-prepared, easily-digestible food containing, when prepared as directed, 140 i.u. of Ostelin vitamin D per cupful.

**Hemolac** (*Cow & Gate, Guildford*). Full-cream milk powder containing 31½ gr. (0.45%) of iron and ammonium citrate to the lb. For prevention of anæmia in infancy.

**Lacidac** (*Cow & Gate, Guildford*). A dried milk with addition of 1 dr. of lactic acid B.P. to 1 pint of milk. Made in two strengths Separated (1% fat) and Half-Cream (16% fat), the optimum dilutions being respectively 1 to 9 and 1 to 8 parts of boiled water. In convalescence, marasmus, eczema, diarrhoea and vomiting.

**Lacquin** (*Cow & Gate, Guildford*). Dried milk containing in 1 teaspoonful 2½ gr. of quinine. For use in the tropics.

**Lacto-Dextrin** (*Battle Creek Food Co., Battle Creek; Coates & Cooper, London*). A carbohydrate food with a high caloric value. Contains 73% of lactose and 25% of dextrin. For changing the intestinal flora, to combat auto-intoxication.

**Lactogen** (*Nestlé, London*) Dried cows' milk to which cream and lactose have been added.

**Mellin's Food** (*Mellin's Food, London*) A malted food in which all the carbohydrate has been rendered soluble.

**Neave's Food** (*Neave's Food, Fordingbridge*). A baked flour containing starch, to be made with milk and water. **Neave's Milk Food** is a dried milk with added lactose and maltose.

**Ostermilk** (*Glaxo Laboratories, London*). No. 1 is the same as Sunshine Glaxo; No. 2 is the same as Full-Cream Glaxo.

**Ovaltine** (*Wander, London*). Composed of malt extract, milk, eggs and converted cocoa, and contains active lecithin. Analysis: Fat 8.01%, soluble carbohydrates 67.9%, nitrogenous substances as protein 14.2%, ash 3.76%, water 1.5%.

**Peptalac** (*Cow & Gate, Guildford*). Pancreatized milk, dextrinized and pancreatized wheat, retaining full mineral and vitamin content with freedom from pathogenic organisms. For use where powers of digestive tract are deficient.

**Plasmon** (*Plasmon, London*). Soluble casein. Nutritive and easily digested Plasmon biscuits, arrowroot, cocoa and chocolate are prepared.

**Savory & Moore's Food** (*Savory & Moore, London*). Wheat flour with addition of malt, the carbohydrate being rendered soluble.

**Secway** (*Trufood, London*). Whey protein (chiefly lactalbumen) 13%, milk sugar 76%, milk salts 9%, fat and moisture of each 1%. In premature and delicate infants.

**Sister Laura's Food** (*Sister Laura's Food Co., Glasgow*). A starchy food to be added to undiluted milk.

**Soluble Protein G.L.** (*Glaxo Laboratories, London*). Soluble sodium salt of casein (protein 91.5%) for use in high protein feeding. Added to skim milk in the proportion of 20 gr. to 1 oz. In fermentative diarrhoea and to increase alkalinity of stools.

**Trufood** (*Trufood, London*). A dried milk without added sugar. Humanised Trufood is also available.

**Starchless Bread** (both brown and white) also biscuits and flour are manufactured. These are generally gluten products (more or less free from starch) and bran foods. Previously they were the only foods available for diabetics. Casein (with eggs and butter) has latterly been employed. Casein bread and biscuits (*Callard & Co., London*) are free from carbohydrates.

It is best to give this casein bread with a weighed quantity of starchy bread when desired. "Gluten bread" may contain as much as 55% of starch. It can be made with 7% of starch, but it is not palatable.

Almonds and other nuts are also used for making bread and biscuits. Various sugarless condiments, foods and drinks are prepared. Saccharin is used as the sweetening agent.

**Sugar-free Milk for Diabetics.** Prepared by a process of separating and washing with warm water, using a dairy cream centrifugal separator. Pour a gallon of cream into a 10-gallon can, fill with water at proper temperature for skimming, and thoroughly stir. Adjust separator to deliver 1 part out of the original 10. The cream is separated and the reservoir and separator bowl rinsed, while still running, by adding more warm water. On repeating the process the cream becomes sugar-free. Flavour restored by addition of salt (0.50 to 0.7%) and a little saccharin (added just before serving).—*J Amer med. Ass*, 1/1921, 792.

The following lists may be useful in assisting the SELECTION OF FOODS FOR DIABETICS:—

(i) Foods free from carbohydrates or containing less than 1%.—Beef, mutton, lamb, pork, poultry, game, sweetbread, tongue, fish, turtle, lobster, eggs, butter, Cheshire, American, Dutch and gorgonzola cheeses, lard, gelatin and starch and sugar-free special foods.

(ii) Foods containing a low proportion of carbohydrates (percentage of carbohydrate is indicated).—Liver 1, sausage (pork) 1, crab 1, crayfish 1, scallops 3, asparagus 3, celery 3, cucumbers 3, lettuce 3, spinach 3, oysters 4, mussels 4, stilton cheese 3, cheddar 4, rhubarb 4, tomatoes 4, mixed pickles 4, cauliflower 5, leeks 6, radishes 6, mushrooms 7, water melons 7.

(iii) Foods rich in carbohydrates.—Milk 5 or more, whey 5, oatmeal (thin gruel) 6, strawberries 7, turnips 8, carrots 9, beet (fresh), cranberries and pineapple 10, oatmeal (boiled), blackberries, dried peaches 11, oranges 12, parsnips, apricots, currants, walnuts and filberts 13, apples and pears 14, macaroni (cooked) 16, calves foot jelly, artichokes, peas (green), cherries and almonds 17, potatoes and pears (dried) 18, figs and grapes 19, plums 20, boiled potatoes 21, bananas 22, rice (boiled) 24, tapioca pudding and cocoa-nuts 28, chocolate 30, mince pie 38, chestnuts (fresh) 42, apple pie 43, bread (brown) 47, potatoes (fried chips) 47, bread (white) 53, rolls 56, lentils (dried) 60, bread (toasted) 61, peas (dried) 62, gingerbread 63, macaroons 65, sponge cake 66, oatmeal 67, chestnuts (dried) 74, sago 78, tapioca 88, arrowroot 97, dried fruits, i.e., apples, apricots, currants, dates, figs, prunes, raisins 62 to 78, meal flour, rice, macaroni, vermicelli 70 to 80.

In the case of list (ii) much of the carbohydrates in some of them is in the form of cellulose, which is not absorbed.

The carbohydrate content of common British fruits and vegetables.—*Spec. Rep. Ser. med. Res. Coun., Lond.*, No. 135, 1929.

**CEREVISIÆ FERMENTUM****B.P.C.****Syn. FÆX MEDICINALIS.**

**Dose.**— $\frac{1}{4}$  to  $\frac{1}{2}$  ounce (8 to 16 g.) of compressed yeast,  $\frac{1}{2}$  to 1 drachm (2 to 4 g.) of dried yeast

The cells and spores of *Saccharomyces Cerevisiæ*

**P.G. VI** requires Fæx Medicinalis to be dried at a temperature not exceeding 40° and to retain its fermenting properties. Compressed and dried yeasts are included in *P. Helv. V.*

All fermentations produced by living organisms (as in the case of yeast fermentation of sugar) are caused by enzymes produced in the cells of the organism. The ferment from the yeast cell was extracted in 1897 by precipitating yeast juice with acetone, centrifuging and washing the sediment with ether and acetone, and drying over sulphuric acid.

The chief species used in the fermentation industries are *Saccharomyces cerevisiæ*, *S. Carlsbergensis*, and *S. monacensis*. Brewer's yeast is a viscid frothy liquid with bitter taste. Baker's yeast or compressed distiller's yeast is obtained by filtering fermenting liquids and compressing the product. Dried yeast is prepared at temperatures not above 30°.

**Uses.** Fresh yeast may be useful in indigestion and flatulence. Both fresh yeast and the dried form are given to check boils and for acne. It is said that fresh yeast given *per os* grows actively in the stomach and slightly reduces sugar in diabetes. Yeast has been used for constipation, as also in tuberculous affections and in dysentery. In dyspepsia due to swallowing nasopharyngeal pus, it acts gastrically, and probably by *direct* contact. It not only checks vomiting, but after 14 to 21 days' use it will be noted that the patient loses the icteric complexion and gets a healthy colour.

Some hold the action of yeast is virtually that of nuclein, as it is still effective after the yeast has been heated to 130° for an hour.

**YEAST EXTRACTS AS FOOD.** These have almost no caloric value. Their chief dietary value lies in their vitamin B content. They are sometimes used to adulterate and enrich genuine meat extracts, which they resemble closely in taste. The chief chemical difference between the yeast and meat extracts is the presence of adenine in the former and creatine and creatinine in the latter.

**Extractum Fæcis (P.G. VI).**

Prepared by first removing the bitterness of fresh "lower" beer yeast with 1% sodium carbonate, and then submitting to a process of auto-digestion in the presence of hydrochloric acid, finally extracting the mass with water, evaporating and incorporating 25% of "medicinal yeast" (entire yeast with bitterness removed) to produce the powder. The extract is used as pill excipient.

**Tabellæ Cerevisiæ Fermenti (B.P.C.)** contain 5 gr. (0.3 g.) of dried yeast.

**Co-Cerevisiæ (Hewlett, London).** Compound yeast tablets containing vitamin B and the glycerophosphates of calcium, potassium and sodium. In septicæmia, pyæmia and neurasthenia.

**Fæxalin (Temmler, Berlin; Coates & Cooper, London)** Dry beer-yeast in the form of flakes. **Dose.**—A teaspoonful to a tablespoonful thrice daily with water, milk or wine.

**Fæxin** (*Martindale, London*) A dry powdered yeast *Dose*—One teaspoonful in water, beer or milk, with meals

**Fæxin Extract** is made by extracting fresh yeast. Used for the various affections for which fresh and dried yeast is employed, e.g., in acne, erysipelas, furunculosis, folliculitis, leucorrhœa, diabetes, conjunctivitis, phlyctenulosa, typhoid and acute articular rheumatism. Available in pills and tablets containing 3 gr.

**Marmite** (*Marmite Food Extract Co., London*). A palatable yeast extract, rich in vitamin B complex. It is stated to promote growth in weakly children, and assimilation of fat, produces leucocytosis in chronic septic conditions and increases general metabolism.

Pernicious anæmia of pregnancy treated with Marmite and with liver extract. Both preparations are active even when the anæmia is complicated by malaria or hook-worm. Marmite thought equal to liver. Suggests that macrocytic anæmia is a deficiency disease.—Lucy Wills, *Brit. med. J.*, 1/1931, 1059

Two cases of megalocytic hyperchromic anæmia associated with tetany and steatorrhœa cured by Marmite, 12 g. daily. Marmite useless in the treatment of Addisonian pernicious anæmia. There is probably a factor common to both liver extract and Marmite, but its determination is not yet possible.—J. M. Vaughan and D. Hunter, *Lancet*, 1/1932, 833

Good results reported from its use in tropical macrocytic anæmia and sprue in India.—Lucy Wills, *Lancet*, 1/1932, 838. See also Sir L. Rogers, *ibid.*, 906

Marmite was found to be an effective alternative to liver extract in the treatment of pernicious anæmia, the hæmoglobin increasing more rapidly than the red blood count in Marmite treatment, while the converse was seen in liver treatment. Dosage was 3 tablespoonfuls per day for primary and relapsed cases, 3 teaspoonfuls for maintenance.—A. Goodall, *Lancet*, 11/1932, 781.

The response to treatment of anæmia with Marmite depends on the ability of the stomach to secrete an intrinsic factor. Thus Marmite was helpful in the cure of the macrocytic anæmia of sprue but not in Addisonian pernicious anæmia.—S. Davidson, *Brit. med. J.*, 11/1933, 481.

In their present form yeast or its products cannot be considered as substitutes for liver, liver extracts or gastric tissue products. The variation in response to treatment with yeast preparations can be explained by definite variations in the degree of failure in secretion of the intrinsic factor.—S. Davidson, *Med. Annu.*, 1935, 20.

**Mycolactine** (*Anglo-French Drug Co., London*) Combination of yeast extract, bile extract and lactic ferments. *Dose*—2 tablets before each meal (constipation, intestinal toxæmia, etc.)

**Mycosin** (*Richter, London*) Desiccated yeast tablets

**Proliferase** (*Anglo-French Drug Co., London*) Suspension of living yeast cells—130 to 140 million cells per ampoule. In ampoules for oral administration in constipation, vitamin B deficiencies, furunculosis, etc.

**Simfax** (*Crookes Laboratories, London*) Pure standardised yeast

**Pulvis Vitamin B<sub>1</sub>** (*B.P. Add.*) Adsorbate of vitamin B<sub>1</sub>.

*Dose*.—Prophylactic, 15 to 30 grains (1 to 2 g.), equivalent to 100 to 200 units per day. Therapeutic, 30 to 90 grains (2 to 6 g.), equivalent to 200 to 600 units.

The adsorbate on fuller's earth of the antineuritic vitamin, vitamin B<sub>1</sub>, containing 100 units of antineuritic activity per g. It is a cream-coloured, tasteless, odourless powder, insoluble in water or acids.

**Preparation.** The vitamin may be obtained from rice polishings, yeast, wheat embryo, etc. From rice polishings it is extracted with dilute sulphuric acid (pH 4.5) in the presence of salicylic acid and toluene as preservatives. The extract is stirred for 48 hours with fuller's earth (3 g. per 100 g. of rice polishings), and the liquid filtered; the precipitate is washed with water and dehydrated alcohol, dried, assayed and adjusted to the requisite strength.

A powder double the above strength (*i.e.*, containing 200 international standard units per g.) is obtainable, also tablets of 0.75 g. containing 150 international units (*Vitamins Ltd., London*).

**Uses.** Claims permissible for vitamin B<sub>1</sub> are that it may be cited as of value in correcting and preventing anorexia of dietary origin in certain cases; that it is of value in securing optimal growth of infants and children and in correcting and preventing beriberi. Because vitamin B<sub>1</sub> is a dietary essential its administration in concentrated form is of value in some conditions where difficulty in utilising ordinary foods in the usual way is encountered. The present status of research on the clinical use of vitamin B<sub>1</sub> for specific diseases other than beriberi and for infant feeding, is such that *definite* claims for therapeutic value in relation to such diseases cannot be recognised. Its use may be indicated, however, in such restricted conditions as pernicious vomiting of pregnancy, tube feedings through a jejunal fistula, and the like, because the above permitted statement applies to such conditions and gives an intelligent basis for such therapy. Claims for concentrates of vitamin B<sub>1</sub>, offered for clinical use, should state the potency in terms of the international unit. The term "concentrate" or a synonym will not be recognised if the product does not exceed a potency of 25 international units per gramme (or per ml.), or if it is a natural product which may have been subjected to a process of dehydration. In connection with medicinal foods acceptable for N.N.R., the claim that a food is valuable because of its vitamin B<sub>1</sub> content may be made only if it provides in the quantity of food consumed daily at least 200 units of vitamin B<sub>1</sub>.—Council on Pharmacy and Chemistry of A.M.A., *J. Amer. med. Ass.*, i/1936, 1733.

There is evidence to suggest frequent deficiency of vitamin B<sub>1</sub> in the human dietary. At the present time only the state of extreme vitamin B<sub>1</sub> deficiency is usually diagnosed. Lesser degrees of B<sub>1</sub> avitaminosis in human beings rarely receive clinical recognition. Experimental results indicate that amounts of B<sub>1</sub> greater than the quantity necessary to protect against extreme deficiency (*i.e.*, beriberi) produce beneficial effects in lesser deficiencies in both animals and man. Results of a previous study indicate a relationship between vitamin B<sub>1</sub> deficiency and disturbances of the carbohydrate metabolism. In a study of 100 cases of clinical neuritis in which vitamin B<sub>1</sub> was administered orally in a dose of 10 mg. daily, 44 were rendered symptom-free, 48 were improved and 8 showed no benefits. In a group of 8 cases of unexplained gastro-intestinal hypotonicity and anorexia, 6 became free from all symptoms on ingestion of vitamin B<sub>1</sub>; 2 were improved. The use of a single agent—pure vitamin B<sub>1</sub>—is urged in the study and treatment of suspected B<sub>1</sub> avitaminosis.—M. G. Vorhaus, R. P. Williams and R. E. Waterman, *J. Amer. med. Ass.*, ii/1935, 1580.

The biochemical lesion in vitamin B<sub>1</sub> deficiency—application of modern biochemical analysis in its diagnosis.—R. A. Peters, *Lancet*, i/1936, 1161.

**NEURITIS in pregnancy.** Four cases successfully treated by oral administration of tablets, each containing 150 units of vitamin B<sub>1</sub>, the dosage being from 10 to 15 tablets daily.—G. W. Theobald, *Lancet*, i/1936, 834.

**POLYNEURITIS.** Marked improvement in a case following parenteral administration of a preparation containing 100 international units per 5 ml.—W. N. Leak, *Lancet*, i/1936, 867.

**Bemax** (*Vitamins Ltd., London*). A stable preparation of wheat germ, standardised to contain 12–15 international units of vitamin B<sub>1</sub> per g., also 3 international units of vitamin A per g., the factors of the vitamin B<sub>2</sub> complex and a high proportion of vitamin E. For constipation, arthritis and conditions of vitamin B<sub>1</sub> deficiency, also in pregnancy and lactation.

**Betaxin** (*Bayer Products, London*). Ampoules containing synthetic vitamin B<sub>1</sub>, 1 ml. containing 1 mg. of the vitamin.

**Ryzamin-B** (*Burroughs Wellcome, London*). A concentrate of rice polishings, supplied in tubes containing not less than 50 i.u. of vitamin B<sub>1</sub> per g.

**Vibex** (*Parke, Davis, London*). Standardised solution of vitamin B<sub>1</sub> prepared from wheat germ, for intramuscular injection. 1 ml. contains not less than 50 Sherman units. *Average dose*.—1 ml. For severe vitamin B<sub>1</sub> deficiency, *e.g.*, beriberi and polyneuritis.

*For further particulars of the chemistry, estimation, etc., of vitamin B<sub>1</sub>, and of the other constituents of the vitamin B complex, see Vol. II*

**Vitamin E.** A vitamin present in wheat germ oil and lettuce; concentrates are usually prepared from the former. Has been found of value in the treatment of habitual abortion, and has also been used in sterility and for thread-worm infestation in children.

Use of vitamin E in 20 cases of habitual abortion and 5 of sterility. Successful in 17 cases of the habitual abortion group and in 2 of the sterility group. Treatment consisted in the administration of 40 drops of wheat germ oil 3 times daily from the 3rd to the 7th month of pregnancy with a dessertspoonful of wheat germ 3 times a day.—P. Vogt-Møller, *Hospitalstidende*, 1933, 76, 621.

Nineteen successful pregnancies and 5 expectant cases (*i.e.*, patients were past the time when abortion usually occurred) out of 27 cases of habitual abortion treated with vitamin E. In 3 cases of threatened abortion similarly treated there were 2 successes and 1 failure. In all of 10 cases of sterility treatment was unsuccessful.—W. Pelton Tew, *Canad. med. Ass. J.*, 11/1934, 521.

Of 29 cases treated, 23 have been delivered and the other 6 are all past the sixth month of pregnancy, the average length of treatment being 5 months. The 23 delivered mothers had had collectively 73 previous pregnancies, resulting in the birth of only 11 living children, 5 of which died immediately after birth. Vitamin E was given in the form of wheat germ oil, 1 3-minim capsule daily *per os*, together with vitamins A and D.—D. W. Currie, *Brit. med. J.*, 1/1936, 752.

**Fertilol** (*Vitamins Ltd., London*) Brand of wheat germ oil. *Dose*.—3 5-minim capsules daily for a minimum period of 3 months recommended.

**Wheat Germ Oil (Collosol Brand)** (*British Colloids Ltd., London*). Wheat germ oil in capsules containing 3 minims (0.2 g.), the vitamin E potency being 40 units as expressed on the Pacini-Linn scale (*i.e.*, 25 mg. daily is required to ensure a litter of rats in a vitamin-E-depleted mother).

**Wheat Germ Oil Extract G.L.** (*Glaxo Laboratories, London*) 3-minim capsules containing the unsaponifiable matter from 5 g. of wheat germ oil.

15 cases of habitual abortion treated with 1 capsule of Wheat Germ Oil Extract G.L. daily for 3–6 months. Successful in every case. 1 capsule daily for a week was successful in removing thread-worms in 34 out of 48 children.—G. C. M. McGonigle, *per Nutr. Abstr. Rev.*, 1934-5, 4, 613.

**Zygon** (*Squibb, New York, Martindale, London*) Wheat germ oil. Also available in 3 m. capsules. *Dose*.—One teaspoonful or 6 capsules daily.

### **Acidum Nucleicum (B.P.C.). Syn. NUCLEINIC ACID**

*Dose*.—1 to 5 grains (0.06 to 0.3 g.). 15 minims of a solution made with alkalis *q.s.*, *v. infra*, hypodermically. Much larger amounts have, however, been given.

Greyish- or yellowish-white powder insoluble in water except in the presence of alkalis, with which soluble salts are formed. Its solution is acid to litmus paper, and liberates CO<sub>2</sub> from carbonates. Insoluble in alcohol and ether.

*When nucleic acid is ordered for injection, give the equivalent in the form of sodium nucleate, the sodium nucleate being prepared from nucleic acid and a sufficiency of sodium carbonate to make it neutral to litmus. A 5% sodium nucleate solution is usually supplied when a saturated solution of nucleic acid is ordered for injection. Sodium nucleate solutions should be prepared with normal saline and a sufficiency of phenol for preservative purposes.*

**Uses.** In treatment of anæmia, scarlet fever and puerperal fever, also in tuberculosis. To increase leucocytosis, and also the resistance of the patient in typhoid.

Sodium nucleate solution 2 ml. containing 0.05 g. per ml. intramuscularly increases leucocyte count; found of value in influenza.—J. Graham Willmore and F. M. Gardner-Medwin, *Lancet*, 1/1922, 116. *See also* Gardner-Medwin,

*Brit. med. J.*, July 12, 1924, and P. S. Hichens and R. E. Gibson. Apparently saved life in a case of imminent pneumonia. 2 ml. given every 4 hours. Should be tried in puerperal fever and other bacterial infections—*Brit. med. J.*, i/1928, 52.

**LOBAR PNEUMONIA.** Sodium nucleate 0.1 g. intramuscularly, of value. It brings down the temperature within 48 hours—otherwise the dose is repeated. Sodium bicarbonate also given by mouth in  $\frac{1}{2}$  drachm doses every 4 hours in severe cases when the urine contains acetone—*Brit. med. J. Epit.*, i/1927, 64.

In lobar pneumonia of an asthenic type in which leucocytes do not rise in number as the disease advances.—J. D. Comrie, *Prescriber*, i/1927, 390.

Pneumonia treated.—H. J. Clutterbuck, *Brit. med. J.*, i/1931, 830.

**SEPTICÆMIA**, where operation is requisite, treated by *B. coli* 50 millions and *streptococcus* 10 million 10 days and again 3 days before operation, and on the night preceding operation, 5 ml. of 5% sodium nucleate intramuscularly.—D. P. D. Wilkie, *Brit. med. J.*, ii/1931, 595.

Sodium cacodylate with nucleic acid in septicæmia, see p. 203.

### Sodii Nucleas.

**Dose** (of 5% w/v solution).—1 to 2 drachms (4 to 8 ml.) orally;  $\frac{1}{2}$  to  $\frac{1}{4}$  drachm (1 to 2 ml.) by injection.

Is used as a 5% solution obtained by treating nucleic acid with sufficient sodium carbonate to form a solution neutral to litmus.

**Nargol** (*Parke, Davis, London*), [P1 81] **Mercuriol** (*Parke, Davis, London*) and **Cuprol** (*Parke, Davis, London*) are compounds of nucleic acid with respectively silver, mercury and copper. Cuprol and Nargol are of use in granular ophthalmia in the form of 5% instillations. Nargol is soluble in water 1 in 4. Contains about 10% of Ag.

### Nuclein.

**Dose.**—15 grains (1 g.) several times daily.

Tablets, 1 grain (0.06 g.).

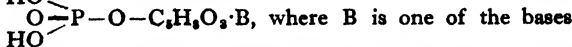
Is considered to be a compound of nucleic acid with albuminates and carbohydrates. It tends to stimulate formation of white blood corpuscles, and hence to act as a bactericide. Septicæmia has been treated with it.

**Acidum Thymenicum.** *Syn. and Prop. Name.* NUCLEOTIN-PHOSPHORIC ACID, SOLUROL (*Allen & Hanburys, London*).

**Dose.**—4 to 6 grains (0.25 to 0.4 g.).

A yellowish-brown powder soluble in water. The solution dissolves uric acid, and has been used in the treatment of gout. It may also be administered by intramuscular injection in 2 gr. doses.

**Pentose Nucleotide** is obtained by the alkaline hydrolysis of the nucleic acid of yeast by means of 1% sodium hydroxide. The resulting solution is acidified and the precipitated acids are purified by means of their lead salts, re-precipitated, and converted into the sodium salts. The latter are used therapeutically as an approximately 8% solution. The preparation probably contains the sodium salts of four nucleotides (compounds containing phosphoric acid, pentose and pyrimidine radicals) of the general formula



guanine, adenine, cytosine or uracil, the pentose present being *d*-ribose.

The solution is administered by intramuscular injection in daily doses of 10 ml. or more in all cases exhibiting a leucopenia or neutropenia, especially in agranulocytic anaemia. In successful

cases the leucocyte count begins to return to normal about 5 days after treatment is commenced.

The treatment of agranulocytic angina would now appear to be the injection of pentose nucleotide, the idea being to stimulate the bone-marrow to produce and liberate granulocytes. The standard dose is 10 ml., containing 0.7 g. administered intramuscularly twice daily till white cell count has risen definitely, and then once daily till count has been within normal limits for at least 3 days. Double the dose in desperately ill cases. If reactions occur (dyspnoea, precordial distress, sweating or vomiting) give divided doses into a site previously anaesthetised by Novocain and adrenaline. Description of a case successfully treated—H. L. Marriott, *Lancet*, 1/1934, 448.

Information, based on a recent tour of America, leads to the conclusion that the results are less satisfactory (in agranulocytic angina) than a study of the literature indicates.—S. Davidson, *Med. Annu.*, 1935, 49.

In a series of 4 cases it was given in 1 acute case with benefit and in 3 chronic cases, with benefit in 1 and no effect in 2. In two other cases its use had to be abandoned owing to the severity of the reaction—one patient, who had previously been in a good condition, passed into a stuporous state and died. It will be agreed by those who have experience of pentnucleotide that the reactions are not infrequently severe enough to prohibit further use of the drug. One reason that we have not been more fortunate in this country (as compared with America) may be insufficient dosage—in severe cases it seems desirable to inject 50 ml. a day. It is hoped that some means will be found to abolish the unpleasant side-actions of the drug so that doses of this order can be given with safety.—L. J. Wits, *Proc R Soc. Med.*, 1936, 29, 680.

**Pentide** (Allen & Hanburys, London), **Pentnucleotide** (Syn. NUCLEOTIDE K. 96) (Smith, Kline & French, Philadelphia, Menley & James, London) and S.P.N. (Evans, Sons, Lescher & Webb, Liverpool) are preparations of sodium pentose nucleotides.

#### Glutathione.

A tripeptide containing glutamic acid, cystine and glycine, corresponding to  $C_8H_{17}N_3O_8$ . M.p.  $190^\circ$  (with decomposition).

The tissues of rat sarcoma, carcinoma and human mammary carcinoma contain abnormally small amounts of reduced glutathione. Glutathione promotes the oxidation of certain unsaturated fatty acids and lecithin.—*J. biol. Chem.*, Oct., 1929, 269.

## CHLORAL HYDRAS

*B.P.*, *U.S.P.* XI, *P.G.* VI, *P. Ned.* V, *P. Jap.*, *P. Helv.* V, *P. Ital.* V, *P. Belg.* IV, *F.E.* VIII, *P. Dan.*

$CCl_3CH(OH)_2 = 165.4$ .

Syn. TRICHLORETHYLI DENE GLYCOL

[P1] "Chloral hydrate."

**Dose.**—5 to 20 grains (0.3 to 1.2 g.) in aqueous solution or in chloroform water, well diluted. *P. Helv.* V and *P. Dan.* have max. single dose 45 grains, max. during 24 hours 90 grains. *Fr. Cx.* has 60 and 180 grains.

Colourless, non-deliquescent crystals, volatilising slowly in air. It liquefies at  $50^\circ$  to  $58^\circ$ .

**Soluble** 4 in 1 of water, 5 in 1 of alcohol, 2 in 1 of glycerin, 2 in 1 of ether, and 1 in 3 of chloroform, likewise soluble in oils and fats.

**Incompatible** with alkalis and alkaline salts (e.g., soluble barbitone), ammonium salts, potassium iodide or permanganate, and with alcohol—chloral-alcoholate may separate. Liquefies with camphor, *q.v.*, and with quinine salts.



**Antidotes.** Empty stomach by emetic or by stomach tube, using at least 2 gallons of water at 105°F. Keep patient lying down and warm with hot blankets and hot-water bottles; he must be roused but *not* walked about. Give hot, strong coffee; aromatic spirit of ammonia,  $\frac{1}{2}$  dr. in 4 oz. of water. Caffeine sodium benzoate, 2 gr., and strychnine,  $\frac{1}{2}$  gr. hypodermically. Oxygen, or oxygen with 7% carbon dioxide, inhalations may be needed, also artificial respiration.

**Uses.** As a hypnotic, it is often combined with opiates, morphine or bromides. Has been used to control the fits of puerperal eclampsia, often in conjunction with morphine, also in insanity and delirium tremens. Its use is contraindicated in heart affections, Bright's disease, and when the vital force is very weak. Is used externally as an anodyne and counter-irritant in liniments for rheumatism, sciatica, etc.

In **ASTHMA** chloral hydrate 30 to 40 gr. is often useful —Yeo

**CHOREA** has been treated by inducing prolonged sleep with its aid. It is given in tetanus. In epilepsy small doses may be efficacious

In **PUERPERAL ECLAMPSIA.** Control of fits by chloral and morphine regarded in France as almost specific.—For details see *Brit med J*, 1/1912, 1128

**SEA-SICKNESS** has been treated with drachm doses of a mixture of 2 drachms of syrup of chloral with 30 grains ammonium bromide, in water 1½ ounces

**INFLUENZA** has been treated with 2% solution as gargle

Clinical trials showed that chloral hydrate in therapeutic doses has no harmful effect on the heart. It is a remarkably effective hypnotic almost entirely free from habit formation. Its use is best avoided in the presence of gastro-intestinal irritation, though this drawback can be practically eliminated by diluting sufficiently with water. When the blood pressure is lowered during chloral hydrate administration the effect is not much greater than occurs in natural sleep—actually more than a quarter of the patients in this series were found to have an *increased* blood pressure after taking chloral hydrate —Stanley Alstead, *Lancet*, 1/1936, 938

**INFANTILE CONVULSIONS** controlled by 2 to 4 gr *per os* or 5 grains *per rectum* repeated 2-hourly. When convulsions cease, gradually reduce dose to  $\frac{1}{2}$  gr twice daily, then give calcium chloride 15 to 30 grains 4-hourly for 3 days —*Per Lancet*, 1/1932, 897

[P1] **Chloral Camphoratum (B.P.C.)** *Syn.* PIGMENTUM CHLORAL ET CAMPHORÆ (T.H.), CHLORAL CUM CAMPHORA.

Chloral hydrate 1, camphor 1. (Measures 1½ by volume.)

It remains liquid at ordinary temperatures, and forms a valuable application painted on painful parts in neuralgia and rheumatism. It mixes freely with alcohol, ether, oils and fats, but not with water or glycerin. [D P1 31] Cocaine 10% or less may be incorporated.

The compound (chloral and camphor) dissolves the alkaloids atropine, morphine and veratrine to the extent of 1 in 30 or more, but their salts are less soluble in it.

[P1] **Chloral Tannin Solution.**

Chloral hydrate 1, tannin 1, melt together on water-bath and dissolve in water, *q.s.* to produce 8. For strengthening the hair

[P1] **Enema Chloralis Hydratis (B.P.C.).** *Dose* —4 ounces (120 ml.).

1 to 3% *w/v* in mucilage of starch

[P1] **Hausst. Chloral. (N.I.F.).**

Chloral hydrate 20 gr., potassium bromide 30 gr., liquid extract of hyoscyamus 5 m., syrup 2 dr., water to 1½ oz.

[P1 §1] **Liquor Bromidi Compositus (B.P.C.).** *Syn.* LIQUOR BROMOCHLORAL COMPOSITUS.

*Dose.*— $\frac{1}{2}$  to 2 drachms (2 to 8 ml)

1 drachm contains 15 gr. each of chloral hydrate and potassium bromide with extract of cannabis and liquid extract of hyoscyamus

Resembles [P1 §1] **Bromidia (Battle & Co., St Louis, Mo.; prepared in England by Roberts & Co., London)** which is stated to contain in each ounce chloral hydrate 91 gr, potassium bromide 91 gr, extracts of cannabis and of hyoscyamus 1 gr each. *Dose*— $\frac{1}{2}$  to 1 drachm in syrup or water

[P1] **Lotio Chloralis Hydratis (Mid. H.).**

Chloral hydrate 10 gr, castor oil 30 m., alcohol (90%) 1 dr, water to 1 oz  
For pityriasis capitis

[P1] **Pigmentum Chloralis et Camphoræ Compositus (B.P.C.)** contains equal weights of chloral, camphor and phenol.

[P1] **Pigmentum Chloral Compositum.** *WH* has chloral hydrate 1, menthol 1, thymol 1, camphor 3 *R.D.H.* is the same, with name Linimentum Chloral Compositum *L.H.* consists of equal parts of chloral hydrate, menthol and camphor

Cautiously used it is good for minor cases of flexural prurigo—one or two drops rubbed into the spots at bed-time.—*W. J. O'Donovan, Brit. med. J., ii/1930, 957.*

[P1] **Nohæsa (Homburg Pharma, London)** Camphor-chloral-menthol with Kamillosan (*qv*) and calcium chloride Ointment for use in hæmorrhoids Also supplied in suppositories

[P1] **Suppository of Chloral.**

Chloral hydrate 5, oil of theobroma 10 Press into moulds Heat must not be applied It is useful in infantile convulsions, but is irritating locally.

[P1] **Syrupus Chloralis (B.P.C.)** *Dose*— $\frac{1}{2}$  to 2 drachms (2 to 8 ml)

Chloral hydrate and water *a. a.* 20% in syrup; 1 dr. contains about 11 gr

[P1] **Tablets of Chloral**, 5 and 10 grains (0.3 and 0.6 g) to be dissolved—not swallowed whole which might cause blistering. *Dose*—1 or more.

**Somnos (Sharp & Dohme, London).** Elixir containing 5.5% of chloral glycerolate. Less depressing to the heart, circulation and respiration than chloral hydrate *Dose*—(*Sedative*) 1 or 2 teaspoonfuls in a glass of water, *Hypnotic*.—1 or 2 tablespoonfuls. Infantile convulsions, colic, chorea, whooping cough, etc., and *per rectum* as hypnotic in post-operative cases and in spasmodophilia.

**Chloralformamidum (B.P.C.).** *Syn.* CHLORALAMIDE.  
 $\text{CCl}_3 \cdot \text{CH}(\text{OH}) \cdot \text{NH} \cdot \text{COH} = 192.4$

[P1] "*Chloral formamide.*"

*Dose*—15 to 45 grains (1 to 3 g.) in weak spirituous or acidulated solution. Max. single dose 4 g., max. in 24 hours 8 g.

In colourless, odourless, shining crystals with a faintly bitter taste. **Soluble** 1 in 21 of water, 1 in 2 of alcohol, 1 in 12 of glycerin; readily soluble in ether and acetone. Hydrolyses when heated with water above 60°. M.p. 114° to 115° (*B.P.C.*), but commercial samples commonly melt at 118°. Incompatible with alkalis, giving chloroform, ammonia and a formate.

**Antidotes.** Treat as for poisoning by chloral hydrate.

**Uses.** Hypnotic in insomnia of alcoholism, neuralgia, hysteria, cardiac diseases and sea-sickness. Chloralamide and potassium bromide of each 15 grains, with orange tincture and chloroform water recommended. It acts if given as an enema.—*Hale White*

[P1] **Elixir Chloralamidi.** *Dose.*—1 ounce (30 ml.) = 30 grains (2 g.). Chloralamide 2 g, alcohol 5 ml, aromatic syrup 5.4 ml., glycerin 15 ml., water *qs* to 30 ml.

[P1] **Hausst. Chloralamid. Co. (N.I.F.).**

Chloralformamide 20 gr., potassium bromide 15 gr spirit of chloroform 20 m, water to 1½ oz.

[P1] **Chlorobrom** (*Burgoyne Burbidge, London*). *Dose*.— $\frac{1}{2}$  to 1 ounce. Contains 30 gr. each of chloralamide and potassium bromide in an ounce, flavoured with liquorice. For insomnia and sea-sickness.

**Butylchloralis Hydras** (*B.P.C.*). *Syn.* TRICHLOROBUTYLIDENE GLYCOL, CROTON-CHLORAL HYDRATE (formerly so-called).

$\text{CH}_3\cdot\text{CHCl}\cdot\text{CCl}_2\cdot\text{CH}(\text{OH})_2 = 193\cdot4$ .

[P1] "*Butyl chloral hydrate.*"

*Dose*.—5 to 20 grains (0·3 to 1·2 g.), in mixtures, pills or cachets.

This body is produced by the addition of water to liquid butylchloral, which is the final product of the action of chlorine on aldehyde. In pearly-white crystalline scales with pungent odour resembling that of chloral hydrate, and an acrid, nauseous taste.

**Soluble** 1 in 43 of cold water, 5 in 3 of alcohol 90% (forming an alcoholate), 1 in 20 of chloroform, 1 in 1 *w/w* of glycerin, 1 in 20 of olive oil and 1 in 2 of ether.

**Incompatible** with alcohol. Butylchloral alcoholate will be formed, and in case of some mixtures will be precipitated.

Menthol 2, with butylchloral hydrate 1 part, liquefy. Combines also with phenazone, *q.v.*

**Uses.** Hypnotic, but weaker than chloral and more depressing to the heart. Given for insomnia not due to pain. In combination with phenazone, cannabis or gelsemium, butylchloral is useful in migraine; neuralgia of nerves other than the cranial is rarely benefited.

[P1] **Mistura Butylchloralis.**

Butylchloral hydrate 4 grains, glycerin 15 minims, water to 1 ounce

[P1-81] **Pilula Butylchloralis cum Gelseminina.** NEURALGIC PILLS. Gelseminine hydrochloride  $\frac{1}{10}$  gr. (0·0003 g.), butylchloral hydrate 3 gr (0·2 g).

[P1-81] **Tablets** are also prepared. For facial neuralgia 2 at the outset followed by 1 hourly until 6 have been taken

[P1-81] **Pilula Butylchloralis cum Camphora et Gelsemio.**

Butylchloral hydrate 2 gr, camphor 1 gr, alcoholic extract of gelsemium  $\frac{1}{2}$  gr, powdered acacia  $\frac{1}{2}$  gr, powdered tragacanth  $\frac{1}{2}$  gr, powdered liquorice 1 gr syrup *q.s.* Varnish. Use similar to the last mentioned

**Chlorbutol** (*B.P.*). *Syn. and Prop. Name.* CHLORETONE (*Parke, Davis, London*), ACETONE-CHLOROFORM (*P. Ital. V, F.E. VIII, P. Belg. IV*), CHLOROBUTANOL (*U.S.P. XI*).

*Dose*.—5 to 20 grains (0·3 to 1·2 g.) in cachet, capsule or tablet, followed by a draught of water or milk, or suspended in a mixture. *U.S.P. XI* average dose 10 grains.

It consists of trichloro-*tert.*-butyl alcohol,  $(\text{CH}_3)_3\text{C}(\text{CCl}_3)\cdot\text{OH} = 177\cdot4$ , with a variable proportion of water of crystallisation. Samples usually contain about  $\frac{1}{2}\text{H}_2\text{O}$ .

**Manufacture.** This compound was discovered by Willgerodt in 1886. It is prepared by adding potash to a mixture of chloroform and acetone, and fractionally distilling.

White crystals, with camphoraceous taste. The anhydrous substance has a m.p. of 96°; the *B.P.* requires not lower than 78°. It volatilises with heat. **Soluble** 1 in 125 of water, 1 in 10 of glycerin, 3 in 2 of alcohol 90%, 1 in 30 of liquid paraffin, 1 in 12 of olive oil.

**Antidotes.** Treat as for poisoning by chloral hydrate, see p. 356

**Uses.** Local anæsthetic and antiseptic and slightly hypnotic. Acts particularly on the stomach. Solutions in liquid paraffin 1 to 2% have been used for inflammation of the middle ear. Vaginal pruritus has been treated with a warm douche 0.4%. For piles, 5 grains in a 30 grain suppository, for a dusting powder for wounds and scalds use chlorbutol 23, with zinc oxide 120, and French chalk 90 parts. 10% may be added to Linimentum Calcis for burns. Capsules, 5 grains, check sea-sickness and other vomiting, and are useful in chorea.

POST-OPERATIVE VOMITING and shock prevented. Value proved by 15 grains in a cachet where time permitted, administered 1½ hours beforehand to every adult operated on.

SEA-SICKNESS. Should be given either in solution or limited to 10 grains daily with intermissions when extended over several days. Satisfactory when given in oil or paraffin or in cachet when taken with moderation—*Lancet*, 1/1913, 1375.

DYSMENORRHOEA well treated with Chloretone 5 grains two or three times daily for a week before period—*Brit. med J. Epit*, 1/1926, 13.

NERVOUS VOMITING and vomiting due to pertussis. Effective dose 0.05 g. Drowsiness which may develop after 8 or 10 days' medication counteracted by adding 0.015 g. caffeine—*P. Freud, J. Amer. med. Ass.*, 11/1929, 1181.

Sea-sickness, whooping cough, conjunctivitis and hay fever. In the latter inhaled as a spray from an atomiser, the solution immediately allays symptoms, the effect lasting many hours. Occasional repetition will carry the patient through distress in early summer. As an anti-spasmodic in acute gastric flatulence, dysmenorrhœa, hiccough, or the pain of shingles—*W. E. Wynter, Lancet*, 11/1929, 1245.

TETANUS successfully treated by Chloretone in dose varying between 30 and 120 grains per rectum in olive oil, and antitetanic serum. The Chloretone injections reduced rigidity of the jaw—*Brit. med J.*, 11/1910, 1402.

Chloretone in 20 grain doses 3 or 4-hourly best for painful spasms—*C. Worster-Drought, Lancet*, 1/1926, 726.

**Nebula Chlorbutolis Composita** (*St. T. H.*) Chlorbutol 15 gr., camphor 40 gr., menthol 40 gr., oil of cinnamon 8 m., liquid paraffin to 3 oz.

**Solutio Chloretonæ Composita Inhalans.** *Syn.* SOLUCION DE CLORETONA COMPUESTA INHALANTE, *FE VIII*

Chloretone 1 g., camphor 2.5 g., menthol 2.5 g., cinnamon oil 0.5 g., liquid paraffin 93.5 g.

**Syrupus Chloretone** (*St. G.H.*).

Chlorbutol 5 gr., saccharin ½ gr., tincture of orange 30 m., glycerin to 1 dr.

**Boro-Chloretone** (*Parke, Davis, London*) Chloretone and boric acid. Antiseptic and analgesic dressing powder for use in eczema, urticaria, etc.

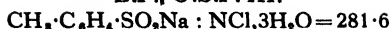
**Chloretone Inhalant** (*Parke, Davis, London*) contains Chloretone 1 g., menthol 2.5 g., camphor 2.5 g., oil of cinnamon, *U.S.P.* (oil of cassia) 0.25 g., liquid paraffin to 100 g. A spray solution for use in catarrhal and congestive affections of nose, throat and bronchi.

**Chloretone Compound Ointment** (*Parke, Davis, London*). Chloretone, calomel, hydrastine, hamamelin, in lanolin and petrolatum base. For irritable and inflammatory conditions of the rectum.

**Dentalone** (*Parke, Davis, London*). Chloretone, oils of clove, cassia and wintergreen. Analgesic for treatment of painful and inflamed tooth sockets, etc.

**Mothersill's Remedy** (*Mothersill Remedy Co., London*) and **Zotos** (*Sangers, London*) contain chlorbutol—*cf.* Proprietary Remedies, Vol. II.

**Sedaform** (*Allen & Hanburys, London*) Chlorbutol capsules 5 grains.

**CHLORAMINA***B.P., U.S.P. XI.*

*Syn. and Prop. Names.* CHLORAMINE-T, MIANIN (P.G. VI, P. Belg. IV, F.E. VIII, P. Helv. V, P. Dan.), CHLORAZENE (Abbott, Montreal; Pharmaceutical Products, London), TOLAMINE (Burroughs Wellcome, London), *p*-TOLUENE SODIUM SULPHO-CHLORAMIDE.

*Dose.*— $\frac{1}{4}$  to 3 grains (0·03 to 0·2 g.) has been given with charcoal.

*Solubility.* About 1 in 7 of water, 1 in 2 of boiling water, 1 in 7 of glycerin and 1 in 12 of alcohol. Organic solvents are undesirable. The aqueous solution is faintly alkaline and has a bitter taste. It is insoluble in liquid paraffin, ether, chloroform and benzene. It becomes less soluble on exposure to air, owing to decomposition.

*Incompatible* with alcohol, hydrogen peroxide and many other substances. Should not be mixed with other antiseptics.

*Uses.* For treatment of infected wounds and as a general surgical antiseptic, mouth-wash, vaginal douche and for urethral irrigation. It is non-irritant and practically non-toxic; does not coagulate blood serum. Not suitable for intravenous use—has marked hæmolytic action. 2% is used for infected wounds—increased to 4%. Mouth-wash, nasal or vaginal douche or for urethral irrigation, 0·25 to 2%.

Mouth and jaw wounds treated with 2% solution. Non-irritant. Results in seven cases good—A. R. Fisher, *Brit. med. J.*, 1/1916, 87.

Bactericidal power of chloramine and hypochlorites in presence of serum is comparatively weak (*cf.* Flavine) and they interfere with phagocytosis—C. H. Browning and colleagues, *Brit. med. J.*, 1/1917, 76.

In aqueous solution it is fatal in 10 minutes to the following organisms at the stated dilutions. *streptococci*, 1 : 34,000; *B. coli*, 1 : 18,000; *C. diphtheriæ*, 1 : 30,000; *pneumococcus*, 1 : 22,000; *B. dysenteriæ*, 1 : 22,000; *B. typhosus*, 1 : 20,000; *staphylococci*, 1 : 18,000.

To sterilise water 1 in 250,000 is effective if a little citric acid (0·8 g. per litre) is added—the resulting water is not unpleasant to taste—*cf.* Halazone.

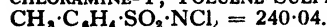
Bilharzia-infected water treated with chloramine—H. S. Blackmore, per *Trans. R. Soc. trop. Med.*, Nov., 1928, 297.

**Carbasus Chloraminæ** (B.P.C.) contains from 4 to 6% of chloramine. A 35% gauze is also made—the former for general use; the latter as preliminary dressing of a wound.

Use dry and subsequently moisten if necessary when in position.

**Chloramine Ointment.** Chloramine 10, sodium stearate 86, water 4. As a dressing to a wound after it has become superficial and is healthily granulating. The chloramine content may be increased to 12% or reduced to 6%.

**Dichloramina** (B.P.C., F.E. VIII, U.S.P. XI). *Syn.* Dichloramine-T, TOLUENE-SULPHODICHLORAMIDE.



Yellow crystals or crystalline powder with odour resembling chlorine. Decomposes on exposure to air with evolution of chlorine. M.p. about 78°.

*Soluble* 1 in 1 of chloroform, 1 in 1 of benzene, 1 in 3 of carbon tetrachloride, glacial acetic acid, chlorinated paraffin or eucalyptol.

This substance enables an oily solution to be prepared, the corresponding monochloride being insoluble in oils.

**Uses.** In solution in chlorinated liquid paraffin, or in a mixture of chlorinated paraffin 1 and chlorinated eucalyptol 4, it is used as a disinfectant of the nasopharynx, *e.g.*, in the treatment of meningococcus carriers (1 to 2% solution). 5% solutions may be applied as a spray to wounds, covering with gauze and re-dressing every 24 hours. Solutions are unstable, and should not be kept for more than 2 to 3 days; they must not be used when a precipitate has appeared.

**Chlorinated Eucalyptol.**

Treat eucalyptol 100 ml with potassium chlorate 3 g. and hydrochloric acid (conc.) 10 ml. for 12 hours or longer. Then wash with water and with sodium carbonate solution. Remove the water, add sodium carbonate 3 g., and allow to stand 24 hours. Filter and dry with a little calcium chloride.

**Chlorinated Paraffin.** *Syn.* CHLORCOSANE (*U.S.P. XI*).

A colourless or yellowish oil, slightly soluble in alcohol, miscible with ether, chloroform and benzene. May be prepared by treating liquid paraffin 20 parts with potassium chlorate 0.1 part and hydrochloric acid 0.5 part, in a wide-mouthed glass bottle, and allowing the mixture to stand until chlorine ceases to be evolved, the mixture is placed in direct sunlight until the odour of chlorine and the yellow colour of the chlorinated oil have disappeared, and is then shaken in a separator with a slight excess of sodium carbonate solution, the chlorinated product is separated, washed with water until free from alkali, and dried by means of anhydrous calcium chloride.

***p*-Sulphondichloroaminobenzoic Acid.** *Syn.* HALAZONE.  
 $C_6H_4(SO_2 \cdot NCl_2)COOH = 270.0$ .

1 in 300,000 is sufficient to sterilise ordinarily contaminated water in 30 minutes.

**Soluble** sparingly in water, insoluble in chloroform and petroleum. Soluble also in excess of cold sodium hydroxide solution, but with less quantity or with feebly alkaline salts, *e.g.*, phosphates or borates, hydrolysis occurs.

**Tablets.** To prepare, powder the acid 4, with dry sodium chloride 92 and add dried sodium carbonate 4 (or dried borax 8%). Pass through a No. 40 sieve (no lubricant required or indeed is to be used), and compress into tablets weighing 100 mg.

Each tablet so made contains 4 mg. of the disinfectant—sufficient for a litre or a quart of heavily contaminated water.

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## CHLORINUM

**Liquor Chlorig** (*B.P.C.*). *Syn.* AQUA CHLORIG. An aqueous solution of about 0.5% *w/v* of chlorine gas.

**Acidum Hypochlorosum.**  $HClO = 52.46$ . Hypochlorous acid, as such, has not been isolated. In solution and especially in the form of its salts—the hypochlorites, *e.g.*, those of calcium and sodium—it has played an important part in many chemical processes.

The acid in dilute solution is practically colourless; in a concentrated form it is yellowish. It readily undergoes decomposition with

formation of chlorine, chloric acid, oxygen and water. It is hence a strong oxidising agent and for this reason a bleaching agent.

The hypochlorites were extensively employed for wound treatment in the war, as described in the following pages.

**Calx Chlorinata** (*B.P., P. Dan.*). *Syn.* SEL DE JAVELLE, CALCARIA CHLORATA (*P. Helv. V*). A dull white powder containing not less than 30% of available chlorine. Solutions of 0.25 to 0.5% applied to burns and ulcers heal them rapidly.

25,000 gallons of water can be sterilised for less than 1d by aid of Calx Chlorinata.—Thresh

Chlorination of potable water. 1 ounce of chloride of lime to 2000 gallons. Remove taste by a few crystals of sodium thiosulphate.—Ministry of Health Circular, *Lancet*, 11/1921, 671

For chlorination of swimming pools see Vol II.

**“Tropical” Bleaching Powder** is available, which is remarkably stable even in hot climates. It consists of bleaching powder mixed with unslaked lime.

**Liquor Calcis Chlorinatæ** (*B.P.C.*). 10%. Contains not less than 2% *w/v* available chlorine, 3% when freshly made.

**Liquor Calcis Chlorinatæ cum Acido Borico** (*B P C*).

*Syn.* EUSOL, LIQUOR ACIDI HYPOCHLOROSI COMPOSITUS

This solution contains when freshly prepared about 0.4% *w/v* of available chlorine

**Uses.** Eusol may be employed as a lotion or on gauze wrung out and applied without waterproof; or as a bath, full strength or diluted. The object is to secure the maximum effect with minimum irritation. As a lotion it should be used *warm*

In presence of blood or any considerable amount of organic matter eusol is worthless —L. P. Garrod, *Brit. med. J.*, 1/1931, 574. It is difficult to reconcile this statement with undoubted clinical value of the preparation.

Eusol was the result of an investigation at the Royal Infirmary, Edinburgh, to prepare an antiseptic which could be applied as a first dressing in the field to prevent sepsis. It has no harmful effect upon the tissues, the effect being purely local. Flow of lymph is induced by it from the tissues. It removes offensive odour in a wound. For field use the antiseptic may also be employed in the form of dry powder (eupad) if water is not available—*vide eupad*.

Has been used undiluted in injuries to the head or hands, lacerated, contused or incised, including cases which are septic, in mastoid operations and in cases of cerebellar abscesses, also for treatment of ulcers of the leg, gangrene of the feet, pyorrhæa alveolaris and follicular tonsillitis. In a wound superficial bleaching may occur with some irritation. If pain is produced, the application is to be diluted with saline. Also used in cystitis by irrigation with 1 in 8 dilution, tuberculous lesions, streptococcal infections and gonorrhœa (1 in 5 dilution). The solution combines

a hypertonicising effect with its antiseptic action. It should not be more than 3 weeks old.

*It must not be applied for long periods to wounds of the back of the hand, dorsum of foot and of the neck, forearm and wrist. In general it should be applied once or, exceptionally, twice daily and should not be covered by protective.*

**BURNS.** Dressings soaked in the following solution. Standard eusol solution 1 part (20%), 10% saline solution 2 parts (sodium chloride 4%), water 2 parts. Dressings must be thoroughly wet when applied and must be changed frequently—W R Wilson, *Brit med J*, 1/1927, 55

**TONSILLITIS** Eusol solution, 1 in 3, or 1 in 4, the most effective of all gargles for tonsillitis, used hourly—H. L. Marriott, *Brit. med. J*, 1/1934, 104

**Eupad.** *Syn.* PULVIS CALCIS CHLORINATÆ ET ACIDI BORICI.

Mix intimately equal weights of finely ground bleaching powder (dry) and powdered boric acid. Should be kept in stoppered bottles and not exposed to the light, in preference mix freshly. Contains about 15% of available chlorine

**Caution.** The evolution of chlorinated vapour in mixing the ingredients is sufficient to "gas" the unwary.

**Uses.** Was employed as a dry dressing to wounds during the war. It evolves hypochlorous acid rapidly when moistened between layers of gauze or lint (as in the pad of a first field dressing) and covered with wool and a bandage. When applied covered with waterproof it should be used for a short time only—10 to 15 minutes as a rule. If it causes pain a weaker application is indicated 1 to 2 g. is suitable in the first field dressing.

**Unguentum Calcis Chlorinatæ.**

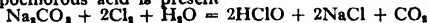
A useful application for chilblains 10% in paraffin ointment.

**Liquor Sodæ Chlorinatæ (B.P.C.).** *Dose.*—10 to 20 minims (0.6 to 1.2 ml.). Contains 2.5 to 3% w/v of available chlorine. *Should be freshly made.*

Formerly used as an antiseptic for wounds and ulcers diluted with 15 to 60 times its volume of water. It is strongly alkaline and Liquor Sodæ Chlorinatæ Chirurgicæ (B.P.) is now preferred for medicinal purposes.

For carbuncles Liquor Sodæ Chlorinatæ, diluted 1 in 20 or 1 in 30, is a non-irritant and powerful dressing.—S Phillips, *Lancet*, 1/1921, 63.

**Eau de Labarraque or Liqueur de Labarraque (Fr Cx)** is about  $\frac{1}{2}$  the strength of Liquor Sodæ Chlorinatæ (B.P.C.). Initially Labarraque made his bleaching solution by passing chlorine into sodium carbonate solution. In this case free hypochlorous acid is present



**Eau de Javelle** (first made in 1789) was originally a solution of chlorinated potash made with potassium carbonate on the same lines as chlorinated soda solution, but it is now replaced in great measure by the soda compound.

**Cataplasma Sodæ Chlorinatæ (B.P.C.).** Linseed poultice prepared with a mixture of solution of chlorinated soda and an equal volume of water.

**Liquor Sodæ Chlorinatæ Chirurgicæ (B.P.).** *Syn.* DAKIN'S SOLUTION.

Prepared from chlorinated lime, sodium carbonate and boric acid, the proportions varying with the amount of available chlorine



in the chlorinated lime. Contains from 0.5% to 0.55% *w/v* of available chlorine. The pH is about 9.5 and the solution is stable for about 3 to 4 weeks. The formula is based on a paper by H. Davis (*Quart. J. Pharm.*, 1931, 360).

**Uses.** A non-irritating antiseptic for wounds. Fresh quantities should be brought in contact frequently.

The solution assists in the dissolution of necrosed tissue, forming soluble chloramines.

Liquor Sodæ Chlorinatæ (B.P.C.), owing to hydrolysis, gives rise to alkalinity, which increases with dilution, hence the boric acid was added with a view to neutralising the caustic alkali as formed.

The solution was first used by *Carrel's Method* (*Brit. med. J.*, 11/1915, 318), rubber tubes with holes throughout their length about 1 cm. apart. Pieces of gauze are placed round and between the tubes, and the solution runs into the wound and irrigates it. Soft paraffin is smeared on the surrounding skin. Cicatrisation is not delayed even by continuous use.

Diluted with 15 to 60 times its volume of water or normal saline it is used as a vaginal douche, for irrigating the bladder and as a mouth-wash. Locally in skin affections 10% to 30% dilutions may be used. *It must not be injected intravenously*

Clockwork-controlled douche irrigates the wound satisfactorily.—C. W. Cathcart, *Brit. med. J.*, 11/1925, 933

BACILLARY DYSENTERY.—Colon lavage of value —H. Jocelyn Smyly, *Trans. R. Soc. trop. Med. Hyg.*, June, 1930, 48

EMPYEMA.—Irrigation with Dakin's solution —*Lancet*, 11/1930, 737.

Closed drainage in empyema. Irrigation with Dakin's solution.—J. D. McEachern, *Brit. med. J.*, 1/1931, 389. See also W. Mitchell, *ibid*, 516.

OIL DERMATITIS is emphatically preventable by the use of an alkaline lotion, e.g. Liq. Sodæ Chlorinat. c. Acid. Boric., as now used in many large engineering works.—W. J. O'Donovan, *Brit. med. J.*, 11/1932, 293.

One of the most common causes of dermatitis is the lubricating oil used in engineering, which gives rise to an acneiform condition. The use of Dakin's solution is a valuable preventive, and buckets of this placed in the wash-places or the shops for immersion of the hands prior to washing, or before commencing work, has reduced the incidence —J. C. Bridge, *Brit. med. J.*, 11/1933, 326.

**Liquor Sodii Hypochloritis (U.S.P. XI).**

A solution of sodium hypochlorite, 4 to 6% NaOCl, which is not suitable for application to wounds.

**Liquor Sodii Hypochloritis Dilutus (U.S.P. XI)**

A modified Dakin's solution prepared by diluting Liquor Sodii Hypochloritis with water, adding sufficient sodium bicarbonate to produce a solution which is no longer alkaline to phenolphthalein, assaying and diluting to contain 0.48% *w/v* of NaOCl.

**Solutio Hypochloritis Sodii ex Dakin (F.E. VIII).** *Syn.* SOLUCIÓN DE HIPOCLORITO DE SODIO, DE DAKIN, is prepared by the interaction of bleaching powder and exsiccated sodium phosphate. The quantities to be employed are stated according to the available chlorine in the bleach. The solution contains 0.45 to 0.5% of available chlorine.

**Liquor Sodæ Chlorinatæ cum Sodii Bicarbonate (B.P.C.)**

*Syn.* DAUFRESNE'S SOLUTION. Contains about 0.45% *w/v* of available chlorine.

**Chlorisol (Allen & Hanburys, London).** Concentrated hypochlorite solution for producing Dakin's solution.

**Fecto (Parke, Davis, London).** Alkaline solution of hypochlorites containing 4% of available chlorine. Disinfectant, deodorant and bleaching agent. Gargle in cases of diphtheria, etc.

**"Milton" Disinfectant** (*Milton Proprietary, London*). Contains sodium hypochlorite 1.01% with sodium chloride 16.8% and small quantities of chlorate, sulphate and carbonate, and calcium chloride. A deodoriser, preservative, insecticide and general antiseptic. It is stated to be harmless to the human system either internally or externally.

It is used for wounds and skin affections, either full strength or diluted down to 1 in 50 or more. For abscesses, fistulas, etc., it can be used undiluted. For the vagina and cervix 1 in 4. Dentures may be cleaned with it by the use of 10 to 20 drops—*not more*—in a tumbler of cold water overnight.

**Magnesium Hypochlorite** is well tolerated by the tissues. Less caustic than the sodium compound. It has less antiseptic power, but twice as much can be used.

To prepare, mix magnesium sulphate 190 g in 2 litres of water and add to chlorinated lime 100 g dissolved in the same amount of water, filter out the calcium sulphate.

## CHLOROFORMUM

*B.P., P.G. VI, U.S.P. XI, P. Jap., P. Helv. V, Fr. Cx, P. Ned. V, P. Ital. V.*

$\text{CHCl}_3 = 119.4$

*Syn* TRICHLOROMETHANE, FORMYL TERCHLORIDE, CHLOROFORMIUM AD NARCOSIN

[P1] "*Chloroform.*"

[83] "*Chloroform—in substances containing less than 10% of chloroform.*"

**Dose.**—1 to 5 minims (0.06 to 0.3 ml.), in mucilage and water, or in a perle; 3 drops = 1 minim. Small doses may be given as chloroform water or spirit of chloroform. Very large amounts (up to 2 ounces) have been taken internally without causing death.

It may be made from ethyl alcohol, acetone, or industrial methylated spirit, and contains 1 to 2% *v/v* of dehydrated alcohol. The alcohol decomposes any phosgene ( $\text{COCl}_2$ ) formed by oxidation, with production of ethyl carbonate and hydrochloric acid.

A little caustic lime added will neutralise any acid products that may form in it. Pink chloroform and green ether have been suggested to prevent accidents.

Chloroform has sp. gr. 1.485 to 1.490. About 15% *v/v* distils below 60°, the remainder at 60° to 62°. Should be kept in amber-coloured, stoppered bottles or in the dark.

**Soluble** about 1 in 200 of water; miscible with alcohol, ether, fixed and volatile oils, and most organic solvents.

**Antidotes** (for poisoning by drinking chloroform). Empty stomach by emetic or stomach tube. Give water freely, with 1 dr. of sodium bicarbonate dissolved in 1 pint. Keep patient lying down. Artificial respiration. Oxygen inhalations. Give 1 oz. of dextrose in 1 pint of hot strong coffee by rectum. No fats for some days; dextrose freely. For treatment of dangerous symptoms arising during anaesthesia, *see* below.

**Uses.** Inhaled, it is anæsthetic and analgesic. Brief inhalations may be used in angina pectoris and in croup. Internally is antispasmodic and sedative for asthma, colic, cough and neuralgia.

In sea-sickness, 1 or 2 drops of chloroform on a lump of sugar or in a wine-glass of iced soda water, repeated every 15 minutes, often give relief.

Externally in liniments to promote absorption and allay pain, as in neuralgia and sciatica. See General Preparations of Chloroform. 1 in 500 is a preservative of infusions and animal extracts. It is a useful deodorant, e.g., for the hands after post-mortem work.

Infection by intestinal parasites, e.g., *Ankylostoma*, *Ascarides* and *Oxiurides* are well treated by doses *per os* of 3 to 4 g. mixed with castor oil or olive oil. A 20 to 30% chloroform ointment is effective against all forms of external parasitic infection.

## ANÆSTHETIC USES OF CHLOROFORM

**Advantages of Chloroform.** (1) It is less irritating than ether vapour, and must therefore be used when there is pulmonary disease. (2) The vapour is not explosive; chloroform can be used when a diathermy needle or cautery is to be employed. (3) It lowers blood pressure so that there is less capillary oozing. (4) It is less volatile than ether and can be used in the tropics.

**Contraindications.** The use of chloroform is not justifiable (1) in cases of grave debility with low blood pressure, especially in cases of patients suffering from shock, (2) in cases likely to develop acidosis, e.g., the diabetic, the sufferer from septic abdomen, and children, (3) in a great many cases during the induction period. To continue to administer chloroform to an excited and struggling patient cannot be made a safe proceeding and is unnecessary and unjustifiable.—A. Mills, *Lancet*, 1/1926, 1134-36.

Chloroform should not be used as an anæsthetic in women at the menopause.—J. H. Hannan, *Brit. med. J.*, ii/1927, 15.

Infants and children take chloroform well, but it should not be used in those with anæmia, sepsis or shock.—J. Ross Mackenzie, *Lancet*, 1/1927, 164.

**Dangers.** The dangerous effects of chloroform fall into four groups: (1) depression of the respiratory centre, (2) fall in blood pressure, (3) late toxic effects, (4) chloroform syncope.

The immediate risk is probably 10 times greater with chloroform than with ether.—J. Ross Mackenzie, *Lancet*, 1/1927, 165.

**ACTION ON THE LIVER.**—Half-an-hour's administration of chloroform caused injury requiring 8 days for recovery. Ether produced definite but transitory effect and nitrous oxide and ethylene none, except with concomitant anoxæmia. Amytal had very little effect and Avertin sometimes produced mild parenchymatous degeneration with occasionally fatty changes.—Wesley Bourne, Sect. of Anæsthetics, B.M.A. Cent. Meeting 1932, *Brit. med. J.*, ii/1932, 319.

**ACTION ON THE HEART.**—Chloroform is a cardiac poison and investigations show that the patient under light chloroform anæsthesia is often in a precarious condition. Undesirable effects on cardiac rhythm are less likely if it is not given to patients who are fatigued, if it is preceded by an injection of morphine and atropine, or if it is administered in the sitting posture or with the head and shoulders raised.—Per *Lancet*, i/1932, 1208. See also E. F. Hill, *ibid.*, 1280.

Anæsthesia in relation to cardiovascular affections.—F. W. Price, *Brit. med. J.*, ii/1926, 879; J. Blomfield, *ibid.*, 883.

**EYE TROUBLES** following anæsthesia. Acute conjunctivitis may be caused by vapour of chloroform or ether, and keratitis with subsequent corneal scarring may occur. Instillation of castor oil prior to anæsthesia, or irrigation with boric acid lotion afterwards, recommended as preventive measures. Keep lids carefully closed and avoid frequent examination.—J. Blomfield, per *Prescriber*, 1926, 142.

**Delayed Chloroform Poisoning** occasionally occurs after recovery from the anæsthetic. Vomiting may persist, or may

commence a day or two after the operation; other symptoms are headache, ketosis, scanty albuminous urine, and jaundice due to fatty degeneration of the liver. Pre-operative starvation and purgation, sepsis and long exposure to the vapour predispose to the condition which usually ends in coma and death. The administration of dextrose before the operation is the chief preventive measure. If the condition arises, administration of dextrose either *per os* or intravenously, together with insulin, may be successful if used early.

**Antidotes for treatment if dangerous symptoms arise during inhalation of chloroform.** Pull out tongue with forceps, remove mucus, etc., from mouth; loosen clothing, begin artificial respiration (20 per minute) at once and keep it up for at least an hour. Keep patient warm and lying down with head well below level of body. Place hot flannels over heart and flap face and chest with the end of a towel. Amyl nitrite inhalations. Strychnine,  $\frac{1}{4}$  gr., or caffeine sodium benzoate, 2 gr., hypodermically. Adrenaline solution, 2 to 3 m, intravenously or into the heart. Heart massage by subdiaphragmatic route.

Reported differences in the action of atropine on the heart in secondary chloroform syncope have been due to differences in mode of injection. It has been injected directly into the heart successfully, in contrast to results reported following injections into the jugular vein — *C R Soc. Biol*, Paris, 1935, 118, 854.

**Administration.** Chloroform is usually administered by a drop-bottle, using the open mask method (*vide* Ether). For induction, the requisite concentration of chloroform vapour is about 2 to 3%, and the mask is held about an inch from the face. The anæsthetic is added slowly at first, the rate being gradually increased until about 30 to 60 drops per minute is being given, after which it is reduced as required. It is advantageous to ensure regular breathing of a proper depth by giving carbon dioxide and oxygen, the mask being placed on the face. Anæsthesia may be maintained by the drop method or, better, by some apparatus such as the Junker bottle, care being taken to see that the bottle connections are correctly made so that the patient receives chloroform vapour and not the liquid. Owing to the decreased amount of blood in the skin in chloroform anæsthesia it is sometimes difficult to observe the onset of cyanosis, and it is often considered advantageous to use oxygen in conjunction with the Junker bottle, the gas being passed through the chloroform.

#### [P1] Chloroform Mixtures.

**A.C.E.** (dehydrated alcohol 1, chloroform 2, ether 3) and **C.E.** (chloroform 2, ether 3) were formerly much used in the belief that they were safer than either chloroform or ether used separately. The ether stimulates the respiration and also the circulation, thus counteracting the effects of the chloroform. For abdominal operations, the addition of chloroform to ether ensures the requisite shallow breathing being obtained without the profound depth of anæsthesia necessary with ether alone, provided pre-anæsthetic sedatives have not been given. The disadvantage of

the mixtures is that owing to the difference in the rates of evaporation of the constituents the composition of the vapour inhaled by the patient is quite different from that of the liquid mixture. With C.E. mixture the patient inhales alternately almost pure ether and almost pure chloroform. Approximate uniformity in composition may be obtained by using some form of Shipway's apparatus in which the air or oxygen is passed through separate bottles of the constituent anæsthetic agents arranged in parallel, but mixtures are now rarely used.

#### **Chloroform Analgesia in Labour.**

Capsules containing 20, 30, and 60 minims and encased in cotton wool and silk are made for use by midwives during labour.

Of all the drugs used for the assuaging of the pains of labour, chloroform is the most satisfactory under the prevalent conditions of ordinary domiciliary midwifery, but a limit must be set on the quantity used, and the degree of anæsthesia must be shallow—F Roques, *Lancet*, 1/1933, 179

An investigation on 100 cases at the Queen Mary's Maternity Home, Hampstead, showed that in 84% of cases there was no apparent effect on uterine contractions, while 16% showed a decrease. In 95% there was apparent lessening of pain, voluntary effort was affected in 60%, diminished in 37%, and increased in 3%. 92% of patients expressed themselves in favour of the capsules. In no case was there any ill effect on the child. Nine of the cases became excited under the chloroform, in 6 cases there was delay in the second stage, and in 8 cases loss above normal during the third stage. It would seem established that the use of chloroform capsules by midwives in the second stage of labour is both safe (but not when the midwife is conducting the case alone) and in the majority of cases beneficial to the patient. The average number of capsules used was 3.41 and the average interval between each capsule 10.16 minutes.—Arthur Rees, *Brit. med. J.*, 1/1933, 241.

The capsules have been an enormous boon in the obstetric departments of L.C.C. hospitals—E. W. Masterman, *Brit. med. J.*, 1/1933, 347. No bad effects in 861 cases, save that 5% of patients became noisy. Labour was not prolonged—Letitia Fairfield, *ibid*

Chloroform by any method should not be used by midwives acting alone. This conclusion has been reached with regret, but both the immediate and delayed dangers which are well recognised occurred in this investigation, and it is not possible fully to guard against such occurrences if the administration of chloroform is in inexperienced hands.—Report on Investigation by the College of Obstetricians and Gynæcologists at the request of the National Birthday Trust Fund, *per Lancet*, 1/1936, 283

### **GENERAL PREPARATIONS OF CHLOROFORM**

**Aqua Chloroformi** (B.P., *P. Jap.*). 1 in 400 of water. *F.E. VIII* and *P. Ital. V*, 1 by weight in 200. *U.S.P. XI* has a saturated solution.

*Dose.*— $\frac{1}{2}$  to 1 ounce (15 to 30 ml.).

Salts, like sodium sulphate, are apt to cause deposition of chloroform from aqueous solution.

**Aqua Chloroformi Concentrata** (B.P.C.). *Dose.*—6 to 12 minims (0.4 to 0.8 ml.). 1 in 10.

**Aqua Chloroformi Duplex** (B.P.C.). *Syn.* AQUA CHLOROFORMI FORTIOR. *Dose.*—2 to 4 drachms (8 to 16 ml.). 1 in 200.

[P1] **Chloroformum Camphoratum** (B.P.C.). Camphor 2 (by weight) dissolved in chloroform 1 (by volume).

Useful for toothache, applied on cotton wool.

[P1] **Chloroformum Mastiche.**

Mastiche 1, chloroform *q.s.* to 2.

**Emulsio Chloroformi (B.P.C.).** *Dose.*—5 to 30 minims (0.3 to 2 ml.).

Chloroform, 1 in 20, with tincture of quillaia, mucilage of tragacanth and water. It is of the same strength as Spiritus Chloroformi.

[P1] **Guttæ Chloroformi cum Menthol Compositæ** —SELF-INFLATOR DROPS. Menthol 15 gr., chloroform  $\frac{1}{2}$  oz., acetic ether and alcohol 90% of each 2 dr — Dundas Grant.

*Directions.*—2 or 3 drops to be placed upon the wool in the inflator on each occasion of use.

**CHRONIC TYMPANIC AND EUSTACHIAN CATARRH.**—Value depends to an extent on the ease with which air containing a little chloroform passes up the Eustachian tubes. Inflation with a Eustachian Self-Inflator is conducted as follows —Drop the amount prescribed on the wool in the mouth-piece with a dropper. With the mouth-piece held firmly between or against the lips (according to the form of the instrument) and the nose-piece tightly in the freer of the two nostrils, compress the other nostril to close it completely. Draw a breath (not through the instrument) and then blow through the mouthpiece so as to puff out the cheeks and “crack the ears.” If vapour is too irritating blow through the instrument a few times before use. To concentrate the effect on the right ear, close firmly with the finger the left ear and bend head sideways over the left shoulder—*vice versa* for the left ear.

The duration of treatment should be controlled by the prescriber.

For the Medicated Politzer Apparatus in which these drops may be used, see Dundas Grant, *Practitioner*, June, 1925.

[P1] **Linimentum Chloroformi (B.P.C.)**

Chloroform 1, liniment of camphor 1.

[P1] **Linimentum Chloroformi (U.S.P. XI)**

Contains at 25° from 40 to 45% w/v of chloroform, and is made by agitating together 3 volumes of chloroform with 7 volumes of camphor and soap liniment.

[P1] **Mist. Tuss. Nig. (N.I.F.)**

Tincture of chloroform and morphine 10 m., liquid extract of liquorice 10 m., water to  $\frac{1}{2}$  oz.

**Spiritus Chloroformi (B.P.)** *Syn.* CHLORIC ETHER 1 in 20 of alcohol 90%.

*Dose.*—5 to 30 minims (0.3 to 2 ml.).

**Spiritus Chloroformi (U.S.P. XI)**

*Average dose.*—30 minims (2 ml.)

Chloroform 8.5 to 9.25% w/v, in alcohol 6% by volume

[P1] **Tinctura Chloroformi Composita (B.P.C.)** *Dose.*— $\frac{1}{4}$  to 1 drachm (1 to 4 ml.) Chloroform 10% v/v with alcohol 90% and compound tincture of cardamom

[P1 81] **Tinctura Chloroformi et Morphinae (B.P.C.).**

*Syn.* CHLORODYNE, TINCT. CHLOROF ET MORPH. (B.P. '85).

*Dose.*—5 to 10 minims (0.3 to 0.6 ml.)

10 minim dose contains chloroform 1  $\frac{1}{2}$  m., ether  $\frac{1}{2}$  m., alcohol 90% 1  $\frac{1}{2}$  m., morphine hydrochloride  $\frac{1}{16}$  gr. (equivalent to 0.18% of anhydrous morphine), and dilute hydrocyanic acid  $\frac{1}{2}$  m., with oil of peppermint, liquid extract of liquorice, treacle and syrup q.s.

Poisoning by 4 ounces of chlorodyne, with recovery by use of atropine, strychnine, and stimulants is recorded.

[D P1-81] **Tinctura Chloroformi et Morphinae Composita (B.P.C.).**

*Dose.*—5 to 15 minims (0.3 to 1 ml.).

Contains 7.5% v/v of chloroform, 1% w/v of morphine hydrochloride and 10% v/v of tincture of cannabis.

10 minim dose contains: chloroform  $\frac{3}{4}$  m., morphine hydrochloride  $\frac{1}{16}$  gr., dilute hydrocyanic acid  $\frac{1}{2}$  m., tincture of capsicum  $\frac{1}{4}$  m., tincture of Indian hemp 1 m.

Contains approximately four times the proportion of morphine present in Tinctura Chloroformi et Morphinae.

[D-P1-81] **Chlor-Anodyne** (*Parke, Davis, London*). Containing in each fluid ounce, morphine hydrochloride 2½ gr., chloroform 46 m., fluidextract of cannabis indica 46 m., dilute hydrocyanic acid 9 m., etc. For use in colic, acute gastro-enteritis, etc. *Dose*.—5 to 15 minims.

## ANÆSTHETIC HYDROCARBONS

**Acetylene.**  $\text{CH} \cdot \text{CH} = 26.02$ .

The initial member of the acetylene series of hydrocarbons (*i.e.*, with triple linkage); a gas with unpleasant odour. It has sp. gr. 0.92 (air = 1). It is compressible into a liquid. This *liquid* form has explosive properties. It is more soluble than ethylene in alcohol.

Acetylene 40% and oxygen 60%, with the addition of oil of pine to mask the smell, used as general anæsthetic. Rapid, simple and safe, but for child-birth, like all other general anæsthetics, its defect is to diminish uterine contractions — C. H. S. Horwitz, *Lancet*, 1/1923, 619.

Give 60% to start with, increase to 70% for full anæsthesia and reduce to 20 or 30% in a long operation. Precede with morphine and scopolamine. — *Lancet*, 11/1923, 240.

Acetylene thought to be an inefficient anæsthetic except in exceptional cases — F. E. Shipway, *Lancet*, 1/1925, 1128.

Acetylene-oxygen may supersede chloroform and ethyl chloride-ether in many operations. Has greater safety, vomiting rare, sense of comfort afterwards, serious sequelæ not observed, but danger of explosion. A 10% concentration will eliminate labour pains without loss of consciousness or diminution of uterine contractions — H. Wieland, per *Prescriber*, 1926, 142.

Acetylene 80%, with oxygen 20%, as a general anæsthetic induced insensibility and muscle relaxation in three minutes. Toxic effect very slight and initial phase of excitation did not occur — *J. Amer med Ass*, 11/1925, 1998.

In dental surgery acetylene of value. — A. Goldman and J. D. Goldman, per *Prescriber*, 1926, 142.

2000 anæsthesias made with acetylene at gynaecological clinic. No deaths, post-operative pneumonia in only 0.3%, and bronchitis in 0.3%. Surpassed in obstetrics all classical types of anæsthesia — per *J. Amer med Ass*, 11/1925, 1437.

**Æthylenum** (*B.P., U.S.P. XI*).  $\text{CH}_2 \cdot \text{CH}_2 = 28.03$ .

*Syn.* OLEFIANT GAS.

The first member of the olefine series of hydrocarbons — *i.e.*, the series in which a double linkage occurs. Ethylene is a colourless gas with slight ethereal odour. It has sp. gr. 0.9784 (air = 1). It burns in air with a bright flame and forms an explosive mixture with 3 vols. of oxygen. At 0° and under a pressure of 42.5 atmospheres it is converted into a colourless liquid which boils at -102°. It is a constituent of illuminating gas.

**Soluble** in 9.2 vols. of water, in 0.5 vol. of alcohol 95% and in about 0.05 vol. of ether, at 25°.

**Uses.** Ethylene is used as an anæsthetic, particularly in America. It is administered with 10 to 20% of oxygen in a manner similar to that of nitrous oxide. It is a more potent narcotic than nitrous oxide, hence more oxygen can be given and greater muscular relaxation obtained without dyspnoea. Recovery is somewhat less rapid than that from nitrous oxide anæsthesia, and transient vomiting may occur. The smell is disagreeable but the senses are soon dulled. It is inflammable, and mixtures with air or oxygen are explosive. Muscular relaxation is less complete than that obtained with ether, but it has no irritant action on the lungs.

For a review of its anæsthetic uses *vide Lancet*, ii/1925, 240. See also E. I. McKesson, *Brit. med. J.*, ii/1926, 1111, C. Langton Hewer, *Lancet*, i/1925, 173; F. E. Shipway, *ibid.*, 1128; J. S. Lundy, *Brit. med. J.*, ii/1926, 1112, and Roy. Soc. Med. discussion, *Brit. med. J.*, i/1930, 862.

The relative toxicity and potency of gas anæsthetics might be expressed as follows. Ethylene being taken as unity nitrous oxide 0.85, acetylene 1.5, propylene 2.25, butylene 4.5, amylene 15—F. H. McMechan, B. M. A. Ann. Meeting, 1926, *Lancet*, ii/1926, 331.

UROLOGICAL OPERATIONS—Ethylene said to be the best anæsthetic, but its use requires a certain amount of experience. The average time for complete anæsthesia is five minutes, and as a rule awakening is without agitation or vomiting. Pantopon subcutaneously before administration suppresses period of excitation—*J. Amer. med. Ass.*, ii/1925, 1742.

Specially suitable in diabetic cases—E. J. Chambers, *Brit. med. J.*, ii/1928, 77.

A survey of 425,000 ethylene anæsthesias shows it is probably as safe as ether, if not safer. The quantity of ethylene capable of explosion is too small to produce considerable damage—M. Salzer, *J. Amer. med. Ass.*, i/1929, 2097.

Much more satisfactory than nitrous oxide—could be used with as much as 20 to 30% of oxygen. Dangerous with cautery or diathermy—I. W. Magill, *Lancet*, i/1931, 353.

For dental work its smell and risk of fire is a disadvantage—R. R. Macintosh, *Brit. Dental J.*, Feb. 15, 1932.

Used with excellent results in a series of 525 operations on children, but use discontinued owing to the "appalling" headaches from which both anæsthetist and surgeon suffered afterwards—R. Jarman, *Brit. med. J.*, ii/1932, 883.

In answer to a questionnaire, no fewer than 757,815 administrations alone, and 267,560 in combination with ether, are recorded—*J. Amer. med. Ass.*, ii/1933, 1716.

**Cyclopropane.**  $\text{CH}_3 \cdot \text{CH}_2 \cdot \text{CH}_2 = 42.05$ .

*Syn.* TRIMETHYLENE.

Cyclopropane, an isomer of propylene ( $\text{CH}_3 \cdot \text{CH} : \text{CH}_2$ ), is heavier than air, with a density of 1.46, and is inflammable and explosive in concentrations of from 20 to 75% when mixed with oxygen. Colourless with a sweetish odour not unlike chloroform or ethylene.

It is not irritating to inhale, induction being smooth and rapid. It does not cause salivation and is rapidly eliminated. Clinically, the anæsthesia resembles that of chloroform but the induction and recovery resemble that of nitrous oxide or ethylene. It is a powerful agent which will produce anæsthesia in low concentration, so it must never be used with small proportions of oxygen in the same way that nitrous oxide and ethylene are used—W. S. Sykes, *Brit. med. J.*, ii/1934, 901.

Cyclopropane seems to be a safe, controllable, non-irritating, non-toxic, anæsthetic, pleasant to take and giving good relaxation. Vomiting followed about as often as with other anæsthetics, but was never severe. No post-operative pneumonia. Its administration requires closed apparatus with carbon dioxide absorption and large supplies of oxygen—Griffith, *Can. med. Ass. J.*, ii/1934, 157.

Cyclopropane unlikely to come into routine use, owing to its three disadvantages. These are (1) the explosibility of anæsthetic mixtures of cyclopropane-oxygen, (2) the increased hæmorrhage from the raised blood-pressure, and (3) the tendency to respiratory depression and even arrest when the deeper planes of anæsthesia are reached. On the other hand, cyclopropane has two great virtues, namely, the extremely high percentage of oxygen compatible with full anæsthesia without premedication, and the absence of irritation to the respiratory passages. These properties rendered the gas particularly suitable for two groups of operations. (1) major thoracic surgery (except when bronchial fistula was present or when lung tissue was to be divided by the diathermic cautery); (2) bad risk cardiac cases, e.g., total thyroidectomy for congestive heart failure. As regards after-effects, Schmidt and Waters, in America, had investigated 2200 cases anæsthetised with cyclopropane-oxygen, and compared them with 2200 similar operations performed under nitrous oxide and oxygen and



ethylene-oxygen, the closed-circuit technique being used in each case. The figures for vomiting and respiratory complications were in favour of cyclopropane, but there were more circulatory complications and post-operative deaths than with the older methods. In order to reduce the risk of explosion, it might be worth while to experiment with the addition of an inert gas, such as nitrogen, as it was possible that a non-explosive three-gas anæsthetic mixture might be evolved.—C. L. Hewer, *Proc. R. Soc. Med.*, Jan., 1936, 262

In spite of some disadvantages, cyclopropane is a valuable anæsthetic agent, and it possesses properties not afforded by other anæsthetics. Its chief sphere of usefulness is for obtaining deep anæsthesia, or for temporarily fortifying gas-and-oxygen. One of the disadvantages of cyclopropane is its cost, but with carbon dioxide absorption technique  $2\frac{1}{2}$  gallons will suffice for an hour's anæsthesia, so that with care the cost per case should not exceed that of other anæsthetics. A real disadvantage is that of capillary bleeding. Induction is always pleasant for the patient, with no sensations of bursting, throbbing or choking, such as are sometimes complained of with other anæsthetics. Although the odour of cyclopropane as it issues from the cylinder is not pleasant, patients are not aware of it during induction, nor do they complain of unpleasant taste or smell during the recovery period such as occurs with ether. Complete abdominal relaxation always obtained although it has often been necessary to increase respiratory exchange by artificial methods. When this is resorted to it must be borne in mind that one is dealing with an extremely potent agent which is not without its effect on the heart muscle. The fact that cyclopropane is neither a respiratory stimulant nor an irritant makes it necessary that the anæsthetist should exercise the greatest care in its administration, but in the hands of the expert it is to be considered an anæsthetic of great utility and value.—S. Rowbotham, *Proc. R. Soc. Med.*, Jan., 1936, 260

**Propylene** and higher homologues as gas anæsthetics. These new anæsthetics show by-effects that, for the present, challenge their safety and utility in clinical anæsthesia. Experiments with methane, propane, pentane and heptane do not offer any hope of a satisfactory clinical anæsthetic.—F. H. McMechan, *Brit. med. J.*, ii/1926, 1106

Propylene as an anæsthetic.—*J. Pharmacol.*, Feb., 1926, 1. See also F. E. Shipway, *Lancet*, i/1925, 1130

**Vinyl Ether.**  $(CH_2 \cdot CH)_2O = 70.05$ . *Prop. Name.* VINESTHENE (Merck, New York; Pharmaceutical Specialities (May & Baker) Ltd., London).

A volatile, clear, practically colourless liquid with a characteristic odour.

B.p.  $28.3^\circ$ ; sp. gr. 0.77. Readily decomposed in air and light into formaldehyde and formic acid, and polymerises to a jelly. Supplied containing 0.01% of phenyl- $\alpha$ -naphthylamine as an antioxidant and also 3.5% of dehydrated alcohol to prevent breath freezing owing to rapid evaporation when used as an anæsthetic.

Successfully used as an anæsthetic. It appears to cause none of the undesirable effects of ether.—S. Gelfan and I. R. Bell, *J. Pharmacol.*, 1933, 47, 1.

The anæsthetic potency is 4 times that of ether and greater than that of chloroform as 1.3 is to 1, and there is a wider "margin of safety" than with ether or chloroform. A few inhalations are sufficient to produce anæsthesia, there is very little excitement, any desired degree of muscular relaxation can be obtained, and recovery is very rapid. Respiration is not interfered with as much as with ether, and tests for liver function show practically no liver change. Results from its use in 50 and 102 obstetrical cases show it to be a very suitable anæsthetic for employment in obstetrics, with minimal danger to mother and child.—Wesley Bourne, *Lancet*, i/1934, 586.

Vinyl ether seems to be particularly suitable for obstetric anæsthesia in general practice on account of its safety for mother and child, its ease of administration, the rapidity of its action, the satisfactory maintenance of any desired degree of narcosis, and the early uneventful recovery. Although vinyl ether may be given with relative safety by the "open drop" method, it is preferable to administer it in a "closed" manner with oxygen.—Wesley Bourne, *J. Amer. med. Ass.* ii/1935, 2047

In man, the evidence up to date shows that vinyl ether is a good anæsthetic, is not irritating to the respiratory passages, usually provides adequate muscular relaxation and shows a remarkable absence of after-effects, particularly vomiting, but greater care necessary to avoid overdosage than with ethyl ether. Until further clinical experience has been gained it should not be used for periods longer than one hour and a half in view of the slight possibility of damage to the liver.—Sir F. E. Shipway, *Lancet*, 1/1935, 82

## CHROMII TRIOXIDUM

*B.P., U S P. XI, P. Helv. V, P.G. VI, P Dan.*

$\text{CrO}_3 = 100.0.$

*Syn.* ACIDUM CHROMICUM, CHROMIC ANHYDRIDE.

In deliquescent, crimson crystals. A powerful oxidising agent.

**Caution:** Incompatible with alcohol, glycerin and other oxidisable substances. **Soluble** about 5 in 3 of water.

**Gargarisma Chromii Trioxidi** (*B.P.C.*). 0.2% w/v.

**Liquor Chromii Trioxidi** (*B.P.C.*) *Syn.* LIQUOR ACIDI CHROMICI

25% w/v in water. Applied to warts, to condylomata and lupus; and 1 in 40 to ulcerated gums and mouth sores. For sweating feet 5 to 10% lotion, in leucorrhœa and ozæna 1 in 2000. In secondary syphilis of the pharynx, the so-called snail-track ulcer treated with a solution (10 grains to the ounce). For mucous and warty patches 5% is useful.

In ulcerative stomatitis the organisms concerned are obligatory anaerobes. Chromium trioxide used warm 1 in 200 to 1 in 400 and applied with wool round a probe relieves pain and removes the necrotic tissue. Immediately after the use of the chromic lotion paint the affected area with a mixture of 20 gr of chlorbutol to the oz. of equal parts glycerin and spirit.

Rodent ulcer treated by chromic acid solution, 10% strength, applied with a brush daily with alternately boric acid and zinc ointment. At first the ulcer may actually increase in size. It is less drastic than arsenic and does not affect healthy tissue cells.—A. Dingwall Kennedy, *Brit med J*, 11/1922, 844.

**CHROMIUM PLATING**—The process consists in wiring the articles to a frame ready for the plating vat, the actual plating (anything up to 15 mins.), unwiring, swilling and polishing. Current 500 to 1000 amps. and 4 to 10 volts. Solution contains 50% of chromic acid. Fumes contain the acid forced up in spray by the evolution of hydrogen at the cathode. Lassar's paste modified with a preponderant base of soft paraffin smeared on hands and arms before work, and a little instilled into each nostril. Soap containing free lanolin used in some works. Dermatitis treatment—double strength calamine solution. When œdema subsides scrub spots with gauze soaked in spirit, dry, and wrap in lint and Lassar's paste. Chromium ulcers should be cleaned and dressed with zinc oxide and soft paraffin. Ulceration of the nose treated with gauze soaked in flavine 1 in 1000.—H. B. Trumper, *Brit. med. J*, 1/1931, 705.

**Potassii Chromas.**  $\text{K}_2\text{Cr}_2\text{O}_7 = 194.2$ . In yellow crystals soluble in water. Used as a reagent.

**Potassii Dichromas.** *Syn.* POTASSIUM BICHRIMATE.

$\text{K}_2\text{Cr}_2\text{O}_7 = 294.2$ .

**Dose.**— $\frac{1}{10}$  to  $\frac{1}{2}$  grain (0.006 to 0.012 g.), in pill with kaolin ointment or in capsule, has been used in dyspepsia and gastric ulcer. Soluble 1 in 10 of water.

**Antidotes.** Empty stomach by emetic or stomach tube. Give magnesia or chalk freely in water. Demulcent drinks. Keep patient lying down and warm; give stimulants if necessary.

Dermatitis may follow the contact of potassium dichromate with the skin of susceptible persons. This may be avoided by frequently rinsing the exposed skin with a saturated solution of sodium bisulphite and then water—*J. Amer. med. Ass.*, 11/1925, 850.

**Acidum Osmicum.**  $\text{OsO}_4 = 254.8$ . *Syn.* OSMIUM TETROXIDE, HYPEROSMIC ACID. *Dose.*— $\frac{1}{4}$  to  $\frac{1}{10}$  grain.

In wax-like yellow crystals. Its vapour is intolerably pungent and attacks the eyes and lungs. Soluble slowly about 1 in 50 of water. It is poisonous and a powerful oxidising body. It is used in microscopy, fat and medullary matter are blackened by it.

Thus and Potassium Osmate 1% solution in 2 to 10 minim doses have been injected hypodermically (painful) for neuralgia, for strumous glands, goitrous swellings, sarcoma, and cancer; also for sciatica and muscular rheumatism, and given internally in epilepsy.

**Liquor Acidii Chromo-Aceto-Osmici** (Flemming's Strong Solution) Mix glacial acetic acid 100 with osmic acid 8 in water 400, and chromium trioxide 15 in water 1500. Cancerous growths have been treated 8 ml. injections at edge of tumour, or 1 ml just beneath its surface. Also for fixing, in histology.

## CHRYSAROBINUM

*B.P., U.S.P. XI, P. Jap., P. Ned. V, P. Helv. V, P. Dan., P. Ital. V, F.E. VIII.*

*Syn.* Commonly but erroneously called CHRYSOPHANIC ACID, ARAROA DEPURATA (*P. Austr.*)

*Dose.*— $\frac{1}{4}$  to  $\frac{1}{2}$  grain (0.01 to 0.03 g.) or more

A yellow, tasteless microcrystalline powder obtained from araroba by extraction with hot benzene. Is a mixture of chrysophanol-anthranol,  $\text{C}_{18}\text{H}_{12}\text{O}_3$ , and related substances

**Soluble** slightly in alcohol 90%, 1 in 16 of ether, 1 in 12 of chloroform, 1 in 18 of benzene, also in fats; almost insoluble in water.

**Uses.** Externally as ointment or pigment. Chrysarobin is a powerful stimulant and parasiticide in acne rosacea, alopecia, psoriasis, lupus, ringworm of the scalp, pityriasis and tinea circinata.

**PSORIASIS**—The only reliable local remedy to remove the eruption with promptitude, but recurrence after its use just as frequent as with other remedies—*B.M.A. Ann. Meeting, Lancet*, 11/1926, 550.

[P1] **Pigmentum Chrysarobini** (*B.P.C.*).

Chrysarobin 10% *w/v* in solution of gutta-percha.

In psoriasis, painted on twice a day with a brush for ten days without washing—finally washing off.

**Pigmentum Chrysarobini et Pyrogallolis**

Chrysarobin 1, pyrogallol 1, ether and alcohol, of each 10, collodion 120. Apply after bathing every third day for psoriasis and ringworm.

[P1] **Suppositorium Chrysarobini.**

Chrysarobin  $1\frac{1}{2}$  gr., iodoform,  $\frac{1}{2}$  gr., belladonna extract  $\frac{1}{2}$  gr., glycerin *q.s.* to make a suitable paste and oil of theobroma *q.s.* to 80 gr. Gives good results in hæmorrhoids.

**Unguentum Chrysarobini (B.P.).**

4% in simple ointment.

It stains the skin and hair, and a strong ointment after three days' continued use sometimes produces feverishness and irritation. 5 to 10 gr. to 1 oz. may be better. Its stains can be removed by benzene, weak solution of potash or chlorinated lime.

**TINEA CRURIS.**—Ung. Chrysarobini *B.P.* will effect a cure in six days if applied thickly on lint twice daily.—*Lancet*, 11/1922, 791.

**Unguentum Chrysarobini (U.S.P. XI)**

Chrysarobin 6, wool fat 5, yellow wax 5, chloroform 4, liquid paraffin 6, yellow soft paraffin to 100.

**Unguentum Chrysarobini Compositum (B.P.C.).**

Chrysarobin 4, ichthammol 4, salicylic acid 2, in yellow soft paraffin to 100

**Unguentum Chrysarobini Compositum (St. J. H.)**

Chrysarobin 25 gr., ichthammol 25 gr., salicylic acid 10 gr., soft paraffin to 1 oz

Psoriasis is treated by an ointment of chrysarobin 5, salicylic acid 2½, oil of birch tar 5, soft soap 6½, soft paraffin 6½

**Chrysarobin Tri-Acetate.** A brownish powder recommended as a substitute for chrysarobin. Solutions of 2 to 3% are said to be effective and free from toxic effects, non-irritant, and do not stain. It is soluble in ether, chloroform and in acetone.

**Araroba (B.P.C.). Syn. GOA POWDER, CRUDE CHRYSAROBIN**

A brownish concretion from the cavities in the trunk of *Andra Araroba* (Leguminosæ), dried and powdered.

Crude araroba is imported from Brazil; it contains about 50% of chrysarobin. The Indian mode of using the drug is to cut a lime fruit, dip it in the powder and dab it on the affected skin. The Brazilians mix it with vinegar. Has been used as an ointment (1 in 16 to 1 in 32 with lard) as a parasiticide.

**Cignolin (Bayer Products, London).**

Dioxanthranol, a synthetic chrysarobin substitute, used as a ¼ to 2% ointment in psoriasis and other skin diseases.

**PSORIASIS**—All cases cleared in 10 to 14 days using Cignolin 10 gr. (in women, and for the face, use 5 gr.), soft paraffin to 1 oz. Rub each of the patches vigorously for 10 minutes once a day. Remove pigmentation by rubbing well with olive oil.—H. W. Cowen, *Lancet*, 11/1932, 267

**CINCHONA****B.P.**

**Dose.**—5 to 15 grains (0.3 to 1 g.).

Consists of the dried bark of cultivated trees of *C. Calisaya*, *C. Ledgeriana*, *C. officinalis* and *C. succirubra* (Rubiaceæ), and of hybrids of either of the last two with either of the first two. It contains not less than 6% of total alkaloids of which not less than one-half consists of quinine and cinchonidine.

**CORTEX CHINCHONÆ P. Helv.** *V* is from *C. succirubra* and contains at least 6.5% of alkaloids

**CINCHONA U.S.P. XI** is from *C. succirubra*, *C. Ledgeriana*, *C. Calisaya* and hybrids. It contains not less than 5% of total alkaloids.

**C. CALISAYA**, *Quinquina Jaune*, is official in *Fr. Cx.* for making extract. 1000 g. of good calisaya bark should yield 30 g. of quinine sulphate (+  $8\text{H}_2\text{O}$ ) = 25 g. approx. of anhydrous quinine sulphate = 22 g. approx. of anhydrous quinine.

**C. SUCCIRUBRA** (*Fr. Cx.*), *Quinquina Rouge*, is required to contain, per 1000 g. of bark, at least 50 g. of total alkaloid = 15 g. of quinine sulphate (+  $8\text{H}_2\text{O}$ ) =  $12\frac{1}{2}$  g. approx. of anhydrous salt = 10.9 g. approx. of anhydrous quinine.

*P. Ital.* V prescribes *Calisaya* or *succirubra* bark containing at least 5% of alkaloids. *F.E. VIII* has *Calisaya*, *Loja* and *succirubra*. *P. Belg. IV* has *C. succirubra* and "other species" containing at least 6.5% alkaloids.

The principal dried barks used for the production of the salts of the cinchona alkaloids are:—Red cinchona bark, from *Cinchona succirubra*, containing 6 to 9% of total alkaloids, 1.5 to 3.5% being quinine; yellow cinchona bark, obtained from *C. Calisaya*, containing 6 to 7% of alkaloids, 3 to 4% being quinine; pale cinchona bark (crown or Loxa bark), from *C. officinalis*, containing about 6% of alkaloids of which half may be quinine; ledger bark, from *C. Ledgeriana*, which may contain up to 10 to 14% of quinine.

The quinine barks, as they are called, now imported from South America, are chiefly the *Calisaya* in quills. A large quantity of bark, the produce of *C. succirubra*, *C. officinalis*, and hybrids, is grown in Madras and other parts of India.

Nine-tenths of the world's supply of bark consists of the rich Java bark, produced by *C. Calisaya* var. *Ledgeriana*.

For further references to the cultivation of cinchona, see 20th Edn., Vol. II, p. 78.

**TERCENTENARY CINCHONA CELEBRATION** (The 300th Anniversary of the first recognised use of cinchona by Europeans.) Addresses on the History of Cinchona by Sir Humphrey Rolleston and Sir David Prain. There are 3000 to 4000 acres under cinchona in India, yielding 40,000 lbs. of quinine per annum. The medical man must determine whether the alkaloids other than quinine are equally efficacious in malaria.—*Brit. med. J.*, 11/1930, 969, 1090; *Lancet*, 11/1930, 1355, 1422; *Pharm. J.*, 11/1930, 621.

**Uses.** The bark in the form of the liquid extract, tincture and its alkaloids has extended use as a bitter tonic. Taken, as such, in powder form it is astringent, giving a feeling of warmth in the epigastrium and occasionally causing vomiting. For further data see the alkaloids quinine, quinidine, etc.

**Decoctum Cinchonæ Concentratum (B.P.C.).** *Dose.*—1 to 2 drachms (4 to 8 ml.). When Decoctum Cinchonæ is prescribed this concentrated decoction diluted with seven times its volume of distilled water may be dispensed.

**Elixir Cinchonæ (B.P.C.).** *Dose.*— $\frac{1}{2}$  to 1 drachm (2 to 4 ml.)

Tincture of cinchona, 1 in  $6\frac{1}{2}$ , in syrup, glycerin and aromatic elixir.

**Elixir Calisayæ** is the same prepared with tincture of *Cinchona Calisaya*.

**Extractum Cinchonæ (B.P.).**

*Dose.*—2 to 8 grains (0.12 to 0.5 g.). Contains 10% *w/w* of cinchona alkaloids.

*Fr. Cx.*—Aqueous extract containing not less than 6% of alkaloids. *P. Ned. V* has 14 to 18% of alkaloids; *P. Ital V* 10%.

**Extractum Cinchonæ Liquidum (B.P.).**

*Dose.*—5 to 15 minims (0.3 to 1 ml.)

Contains 50% *w/v* of extract of cinchona, equivalent to 5% *w/v* of total alkaloids, with hydrochloric acid, glycerin, alcohol and water.

*If prescribed with acid*, as in the following:—Spirit of chloroform 1½ dr., nitrohydrochloric acid 1½ dr., liquid extract of cinchona 1½ dr., water to 6 oz., mix the first three in order as written, and pour into the water to produce best result

Liquid extract of red bark has been much lauded in America for giving drunkards a distaste for alcohol

**Extrait de Quinquina Rouge (Fluide)** (*Fr. Cx. Supp* 1920) is made by percolation with dilute hydrochloric acid and contains 3.5% of total alkaloids *P. Ital V* contains 5% of total alkaloids

**Infusum Cinchonæ Acidum Concentratum (B.P.C.)**

*Dose*—½ to 1 drachm (2 to 4 ml). 1 in 2½

**Infusum Cinchonæ Recens (B.P.C.)**

*Dose.*—½ to 1 ounce (15 to 30 ml) 1 in 20, with 1 in 80 of aromatic sulphuric acid

**Mist. Cinchon. Acid. (N.I.F.).**

Liquid extract of cinchona 10 m, dilute phosphoric acid 10 m, glycerin 10 m water to ½ oz.

**Mist. Cinchon. Ammon. (N.I.F.)**

Liquid extract of cinchona 10 m, ammonium carbonate 3 gr, chloroform water to ½ oz

**Tinctura Cinchonæ (B.P.).** *Dose*—½ to 1 drachm (2 to 4 ml)

Extract of cinchona, 10% *w/v*, in alcohol 70%.

*P. Ital. V* requires not less than 1% of alkaloids.

**Tinctura Cinchonæ Composita (B.P.).** *Syn.* HUXHAM'S

TINCTURE OF BARK. *Dose*—½ to 1 drachm (2 to 4 ml.).

Extract of cinchona, 5% *w/v*, with orange peel, serpentary and cochineal

**Tinctura Cinchonæ Composita (U.S.P. XI)**

*Average dose*—60 minims (4 ml)

Cinchona 10, bitter orange peel 8, serpentaria 2, in alcohol, with glycerin and hydrochloric acid but without cochineal

**Vin de Quinquina Officinal (Fr. Cx.)**

*Dose.*—½ to 5 ounces (15 to 150 ml)

Macerate cinchona 25 with dilute hydrochloric acid 2, alcohol (60%) 75, for 24 hours, shaking occasionally Add red wine 920, macerate 24 hours and filter

**Vinum Chinæ (P. Jap. IV)** *Dose*—1 to 4 drachms. Dissolve gelatin 1, by warming in distilled water 10, and add sherry 1000, cinchona bark in coarse powder 40 Macerate for 8 days; press, and in the expressed liquid dissolve sugar 100, tincture of bitter orange peel 2 set aside in a cool place for 14 days and filter.

**Vibrona (Fletcher, Fletcher & Co, London).** A wine containing the alkaloids of cinchona. A wineglassful contains the combined alkaloids of 5 gr. of cinchona bark in the form of hydrobromides. Total alkaloidal content 0.025%

**Acidum Quinicum.** *Syn* KINIC ACID

$C_7H_7(OH)_4COOH, H_2O = 210$  l.

*Dose.*—4 to 8 grains (0.25 to 0.5 g.)

An acid contained in cinchona, principally combined with the alkaloids and with calcium, forms white crystalline masses, soluble in water about 5 in 6, and in alcohol 90% 1 in 35. It is decomposed into hippuric acid in the system. This and lithium quinate in similar dose are used in gout and rheumatism

**Alstonia (B.P.C.)**

The dried bark of *A. scholaris* (dita bark) from India and of *A. constricta* (Australian fever bark), from Australia (Apocynaceæ). Contains various alkaloids and is used in the East in diarrhoea and as a tonic in malaria. **Infusum Alstoniæ.** *Dose.*— $\frac{1}{2}$  to 1 oz. 1 in 20. **Tinctura Alstoniæ.** *Dose.*— $\frac{1}{2}$  to 1 drachm. 1 in 8.

**Cusparia (B.P.C.).** *Dose*—10 to 30 grains (0.6 to 2 g.). *Syn.* ANGOSTURA BARK.

The bark of *Galipea officinalis* (Rutaceæ). Stimulant and tonic. In diarrhoea, dysentery and dyspepsia much employed in South America and West Indies. The bark is stated to contain cusparine  $C_{20}H_{19}NO_2$ , cuspareine  $C_{18}H_{17}NO_2$ , and galipoidine  $C_{18}H_{17}NO_2$ .

**Infusum Cuspariæ Concentratum (B.P.C.).**

*Dose.*— $\frac{1}{2}$  to 1 drachm (2 to 4 ml.). 1 in 2 $\frac{1}{2}$

When Infusum Cuspariæ is prescribed this concentrated infusion diluted with seven times its volume of water may be dispensed.

## CINCHOPHENUM

*B.P., P. Dan.*

$C_6H_5 \cdot C_6H_5N \text{ COOH} = 249.1$ .

*Syn. and Prop. Names.* ACIDUM PHENYLCINCHONINICUM (*P.G. VI, P. Helv. V, P. Ned. V, P. Bor. VII, P. Svec. X, P. Ital. V, P. Belg. IV, F.E. VIII*), ACIDUM PHENYLCHINOLINCARBONICUM, QUINOPHAN, 2-PHENYLQUINOLINE-4-CARBOXYLIC ACID, AGOTAN (*Howard & Sons, Ilford*), ATOCIN (*Cavendish Chemical Co., London*), ATOPHAN (*Schering, London*), PHENOQUIN (*Southall Bros & Barclay, Birmingham*), TOPHOSAN (*Richter, London*).

[P1] "Phenylcinchomonic acid; salicylcinchomonic acid; their salts, their esters."

[S1] "Phenylcinchomonic acid; salicylcinchomonic acid; their salts; their esters."

[S4] "Phenylcinchomonic acid; salicylcinchomonic acid; their salts; their esters."

*Dose.*—*B.P. Add.* 5 to 10 grains (0.3 to 0.6 g.) *B.P. '32* gave max. dose 15 grains. Is often given with sodium bicarbonate, as in the following scheme. 8 gr. thrice daily after meals. Simultaneously on the first day,  $\frac{1}{2}$  oz. (15 g.) and on the following days 75 gr. to 150 gr. (5 to 10 g.) of sodium bicarbonate in plenty of water.

A yellowish cream-coloured amorphous powder, melting at  $214^{\circ}$  to  $217^{\circ}$ .

**Soluble** 1 in about 120 of alcohol 95%, 1 in about 100 of ether and 1 in about 400 of chloroform. Insoluble in water. It dissolves in solutions of alkali hydroxides, bicarbonates and carbonates.

**Incompatible** with sodium bicarbonate and other alkalis *in vitro*.

#### Toxic Effects of Cinchophen.

Two cases terminating fatally following continued use (three  $7\frac{1}{2}$ -grain tablets daily) Intolerance may be indicated by nausea, loss of appetite and albuminuria. Even if used in the correct intermittent manner it may be dangerous. —L. J. A Lowenthal, W. A MacKay and E. Cronin Lowe, *Brit med J*, 1/1928, 592

Forty-seven cases of cinchophen toxicosis published, with 10 deaths. Evidence of serious injury to liver in all cases. On the appearance of gastric intestinal symptoms, rashes, or icterus, it should be immediately stopped. Its therapeutic use may well be re-evaluated in view of its harmful properties —H. S Reichle, *J. Amer. med. Ass.*, 11/1929, 951.

Fatal case of poisoning. 45 grains a day for 4 days, with intermission for  $2\frac{1}{2}$  months. Death due to acute hepatitis —W Morris, *Brit. med J*, 1/1931, 221.

Should not be used as a routine measure in the treatment of gout. Its use should be reserved for those cases in which other methods have proved inadequate. Details of 35 cases of jaundice following use —T. G Reah, *Lancet*, 11/1932, 504

The widespread use of cinchophen derivatives has become a serious danger. 92 cases of poisoning have been recorded, 40 fatal—probably many cases of non-fatal toxicity are unrecognised and unreported —H. A. Harris, *Brit. med J.*, 11/1932, 707.

A fatal case of subacute yellow atrophy of the liver following taking of  $37\frac{1}{2}$  grains of cinchophen (Atophan) at the rate of one  $7\frac{1}{2}$ -grain tablet on 5 successive days.—T N Fraser, *Brit med J*, 11/1934, 1195

In the eight-year period from 1924 to 1932 inclusive, there were about 660,000 pounds of cinchophen produced and consumed, representing approximately 660 million doses of  $7\frac{1}{2}$  gr. each. Despite this, during this period there were only 38 reported deaths in the United States attributed to the use of this drug, making the chance toxic dose 1 : 17,000,000, which is as low as one could reasonably expect for any active therapeutic agent. Cinchophen is not a harmless drug, but it is a very effective one, and when used with proper care and reasonable precautions, its benefits far outweigh its limitations —R G. Snyder and co-workers, *J Lab. Clin Med*, 1936, 21, 545

**Antidotes.** (Chronic poisoning—from prolonged dosage.) Stop the drug. Keep patient in bed. Dextrose and fluids freely; dextrose and insulin for severe cases.

**Uses.** Facilitates the elimination of uric acid from the organism in gout and rheumatic affections, also used in neuralgia and sciatica. It may cause cloudiness and red colour in the urine.

[P1 81 84] **Tabellæ Cinchopheni** (B.P.C.) contain 5 gr. (0.3 g.).

[P1 81 84] **Acitophosan** (Richter, London). A combination of calcium cinchophen and calcium aspirin. Dose—3 to 6 8-grain tablets daily with plenty of fluids. Influenza, gout and rheumatic affections.

[P1 81 84] **Anotal** (Napp, London). A chemical combination of phenylcinchoninic acid with ethyl urethane. Better tolerated than phenylcinchoninic acid and does not cause gastric upset. Issued in the form of tablets

[P1-81-84] **Atophanyl** (Schering, London). Contains equal parts of sodium Atophan and sodium salicylate in solution

For intravenous injection.—10 ml., containing 0.5 g of each

After injection, the arm should be held above the head for 1 to 2 minutes. Warm the ampoules first. The patient should not undertake undue exertion too soon after the pain has been relieved



*For intramuscular injection.*—5 ml., containing 0.5 g. of sodium Atophan, 0.5 g. of sodium salicylate, and 0.6 g. of Novocain in distilled water To be given deeply in the upper external quadrant of the gluteal muscle

In chronic cases, 10 to 15 injections are given; usually one injection per day for 4 days, followed by an interval of 2 to 3 days Used for the same purposes as cinchophen.

Various rheumatic conditions benefited by intravenous use—*Brit med J Epit*, i/1926, 90.

Atophan intramuscularly or intravenously in cases with a definite rheumatic diathesis is said to give good results in scleritis, iritis, and iridocyclitis injections daily or twice daily—*Brit. med J Epit.*, i/1927, 12

[P1 81-84] **Gorun Cachets** (*T Christy & Co., London*) A combination of cinchophen, hexamine, and glycooll Also in ampoules of solution for intramuscular injection. In sciatica, lumbago, etc

[P1 81-84] **Hexophan** (*Bayer Products, London*) Oxyphenylquinoline-dicarboxylic acid Dose—1 or 2  $\frac{1}{2}$ -grain tablets thrice daily In gout, rheumatism and lumbago.

[P1 81 84] **Lygal** (*Henning, Berlin; Pharmaceutical Products, London*) Phenylquinolinecarboxylate of calcium dimethylaminophenazone (tablets contain the calcium, suppositories and ampoules the sodium, combination) and caffeine sodium salicylate Dose—2 tablets of 0.3 g 2 or 3 times a day, 2 or 3 suppositories of 0.75 g daily, intramuscular or intravenous injection of 2 ml of 30% solution (= 0.6 g) Arthritis and the uric acid diathesis.

[P1-81 84] **Neo-Phenoquin** (*Southall Bros and Barclay, Birmingham*) is lithium phenylcinchoninate  $C_8H_7C_2H_5N COOLi = 255.0$

Dose—From 5 to 10 tablets daily, each tablet containing 0.25 g., after meals, followed by a glass of water For elimination of uric acid in acute and chronic gout

Simultaneous use of sodium bicarbonate is sometimes desirable

[P1 81 84] **Oxyl-Iodide** (*Lilly, London*). Phenylcinchoninic acid hydriodide, containing 33% iodine In arthritis, neuritis and myositis

[P1 81 84] **Piperosan** (*Richter, London*) Phenylcinchoninic acid 6 gr, piperazine  $\frac{1}{2}$  gr. Dose.—1 to 3 tablets daily Pyelitis and renal calculus

[P1 81 84] **Sciatago** (*Coates & Cooper, London*) Dragées containing cinchophen hexamine and glycooll Dose—2 dragées twice daily for 2 or 3 weeks Rheumatism, lumbago, sciatica.

[P1 81 84] **Tophosanyl** (*Richter, London*). Sodium phenylcinchoninate 8 gr, sodium salicylate 8 gr, in ampoules of 5 ml. for intramuscular injection, and of 10 ml for intravenous injection. **Tophosamin** Hexamine phenylcinchoninate in ampoules of 5 ml (= 8 gr active substance) for intravenous injection

[P1 81 84] **"Ung. Agotan Co."** (*Howard & Sons, Ilford*)

Agotan with a rubefacient in ointment form, for use in general, articular and muscular rheumatism, gout, lumbago, sciatica, erythema nodosum, torticollis, pleurodynia, neuritis, urticaria and chilblains. The simultaneous use of Agotan tablets per os increases results

Atophan applied externally as ointment gave good results in chronic rheumatism and lumbago—H Horsters and H Rothmann, per *Prescriber*, 1926, 315. See also *Lancet*, ii/1929, 413.

[P1 81 84] **Atoquinol** (*Ciba, London*) is allyl phenylcinchoninate in tablets containing 4 gr Dose—4 to 8 tablets in 24 hours They should be administered with a large quantity of liquid, and if the urine shows a sediment of uric acid or urates, it is advisable to prescribe sodium bicarbonate as well

It forms odourless yellowish crystals, m p 30°, insoluble in water, readily soluble in ether and oils Has analgesic and antipyretic properties and is used similarly in arthritis, gout, neuralgia, sciatica, etc

It may be applied externally in an ointment (20%)

Renal lithiasis is the only known contraindication

[P1 81 84] **Methyl Phenylcinchoninate**. *Syn. and Prop Name.* METHYL PHENYLCHINOLINCARBONATE (*P. Helv. V, P.G. VI*), METHYLCHINOPHENUM NOVATOPHAN (*Schering, London*).  $C_8H_7C_2H_5N COOCH_3 = 263.1$ .

Dose.—8 grains (0.5 g.) 4 times daily to 15 grains (1 g.) thrice daily. Simultaneously on first day  $\frac{1}{2}$  ounce (15 g.), and on the following day 75 to 150 grains (5 to 10 g.) of sodium bicarbonate.

This compound is the methyl ester of cinchophen and is used similarly. It occurs as yellowish tasteless crystals insoluble in water.

[P 81 84] **Arcanol** (*Schering, London*) Tablets containing Atophan methyl ester  $7\frac{1}{2}$  gr and acetylsalicylic acid  $7\frac{1}{2}$  gr In influenza, etc

**Neocinchophenum** (*B.P.C., U.S.P. XI*) *Syn. and Prop Name.* ETHYL METHYLPHENYLCINCHONINATE, TOLYSIN (*Calco Chemical Co., Bound Brook, N.J.; Martindale, London*).

*Dose.*—10 to 15 grains (0.6 to 1 g) 3 or 4 times daily for 4 or 5 days. It may be necessary to give 100 grains daily in rheumatic fever. *U.S.P. XI* average dose 8 grains.

A yellowish-white crystalline powder, m.p.  $74^{\circ}$  It is the ethyl ester of 6-methyl-2-phenylquinoline-4-carboxylic acid.

*Uses.* An analgesic, antipyretic and uric acid eliminant. Indicated in gout, rheumatism, rheumatic fever, arthritis, neuralgia, neuritis and sciatica. It does not depress the heart, or injuriously affect the kidneys

Efficient in acute rheumatic fever, complete relief of symptoms being usually obtained after 10 to 16 g. 2 g given every 2 hours for 3 doses, followed by 2 g. every 4 hours—H G Barbour, E Lozinsky and C Clements, *Amer. J med Sci.*, 1/1923, 708 See also P J Hanzlik, R. W. Scott and others, *J. Amer med Ass.*, 1921, 1728

Efficacy in arthritis—Chace, Myers and Killian, *J. Amer med Ass.*, 11/1921, 1236.

Advocated for headaches of nephritis—A I Ringer *Amer J med. Sci.*, 1/1921, 814

In acute rheumatic fever—C W Chapman, *Practitioner*, 1/1924, 41  
In rheumatic heart disease Tolysin has definite action, is less toxic than salicylates, and enables the worst cases of carditis to be treated without fear of drug complications—F J Poynton, *Lancet*, 11/1928, 638

Contrasted with control litter mates, no difference could be observed in the growth rate of young rats receiving daily for 100 days 1 g per kilo of Tolysin. Histological evidence of liver damage in these animals is entirely lacking. Complete absorption of daily doses of this size in rats has been demonstrated. Tolysin in this enormous dosage has therefore no toxicity for rats. Similar dosage with cinchophen usually causes death within a few days or weeks, and even those which survive for many weeks exhibit very poor growth curves. Tolysin is far less toxic to rats than cinchophen, which fact accords with the extreme paucity of clinical evidence of Tolysin toxicity—H G Barbour and A Gilman, *J Pharmacol.*, 1935, 55, 400

## CINNAMOMUM

### B.P.

*Dose.*—5 to 20 grains (0.3 to 1.2 g)

The dried inner bark from *C. zeylanicum* (*Lauracæ*).

Aromatic, carminative and antiseptic, employed as flavouring agent. Contains volatile oil and tannin

*P Jap IV* has Cortex Cinnamomi *Loureirii*, *syn.* NIKKEI BARK, Japanese Cinnamon Bark. *Cinnamomum U.S.P. XI* is from *C. Loureirii*. *P. Helv. V* includes both Cortex Cinnamomi *ceylanici* and *chinensis*, Ceylon cinnamon being used for the syrup, while other preparations are made from *C. Cassia* bark.

**Aqua Cinnamomi Destillata** (*B.P.*).

*Dose.*— $\frac{1}{2}$  to 1 ounce (15 to 30 ml.). 1 in 10.

**Aqua Cinnamomi Concentrata (B.P.).***Dose.*—5 to 15 minims (0.3 to 1 ml.).

Contains 2% *v/v* of oil of cinnamon, and is approximately 40 times the strength of the distilled water.

**Pulvis Cinnamomi Compositus (B.P.C.).** *Syn.* PULVIS AROMATICUS.*Dose.*—10 to 60 grains (0.6 to 4 g.).

Cinnamon, ginger and cardamom, equal parts.

**Tinctura Cinnamomi (B.P.C.).***Dose.*— $\frac{1}{2}$  to 1 drachm. 1 in 5.**Tinctura Cinnamomi Composita (B.P.C.).***Dose.*—1 to 2 drachms (4 to 8 ml)

Cinnamon 1 in 40, with cardamom, long pepper and ginger.

**Oleum Cinnamomi (B.P.).***Dose.*— $\frac{1}{2}$  to 3 minims (0.03 to 0.2 ml.).

The light yellow oil distilled from the bark.

Contains 50 to 65% *w/w* of cinnamic aldehyde,  $C_9H_8O$ .

Oleum Cinnamomi (*U.S.P. XI*) is identical with Oleum Cassiæ (*B.P.C.*), from *C. Cassia*. It contains not less than 80% *v/v* of cinnamic aldehyde. *P. Helv. V* includes the oils from each of the two barks.

*Soluble* in alcohol 90% about 10 in 3.

*Uses.* Cinnamon oil is used in influenza and catarrhs, being given in milk or on sugar; is occasionally prescribed as an inhalation (30 to 40 minims) with boiling water 1 pint.

**Solutio Cinnamomi Composita (Brompton H)**

Menthol 4, oil of cinnamon 3, oil of lemon 4, creosote 10, oil of punilio pine 10, spirit of chloroform 10. For use on an oro-nasal respirator

**Spiritus Cinnamomi (B.P.C.)** *Dose.*—5 to 20 minims (0.3 to 1.2 ml) 1 in 10.

**Spiritus Cinnamomi (U.S.P. XI)** *Average dose*—15 minims (1 ml)

Oil of cinnamon (*U.S.P. XI*, see above) 10%, in alcohol

**Cassia (B.P.).** *Syn.* CASSIÆ PULPA. *Dose*—1 to 2 drachms (4 to 8 g.)  
The evaporated aqueous percolate of the pulp of commercial cassia pod.  
*Fr. Cassé en batues* Mild aperient.

**Cassia Cortex.** *Syn.* CHINESE CINNAMON Is the bark of *Cinnamomum Cassia* (Lauraceæ). It contains 1 to 2% of volatile oil **Cassia Flos**, *syn* CASSIA BUD, are the immature fruits, and are used as a spice.

**Cassia Fructus (B.P.C.)** *Syn.* CASSIA POD The ripe fruits of *C. Fistula* (Leguminosæ). The fruit is a dark chocolate-brown pod about 35 to 50 cm long and 18 to 25 mm. in diameter.

**Oleum Cassia (B.P.C.)**

*Dose.*— $\frac{1}{2}$  to 3 minims (0.03 to 0.2 ml.).

Obtained from the leaves and twigs of *Cinnamomum Cassia* Resembles oil of cinnamon but has a less fragrant odour and a harsher taste.

**Canella (B.P.C.)** *Syn.* WILD CINNAMON. The bark of *Canella alba* (Canellaceæ) containing volatile oil. Stomachic.

**Oliveri Cortex (B.P.C.).** *Syn.* BLACK SASSAFRAS From *Cinnamomum Oliveri* (Lauraceæ). Has been used as a substitute for cinnamon.

**Tinctura Oliveri Corticis.** *Dose*— $\frac{1}{2}$  to 1 drachm 1 in 10

## COCA

(with COCAINE and COCAINE SUBSTITUTES)  
B.P.C.

Syn. COCÆ FOLIA (P. Helv. V, P Ital V), CUCA.

[D] "Coca leaves," see p. 1033.

"Cocaine (including synthetic cocaine) and ecgonine and their respective salts, and the esters of ecgonine and their respective salts";

"Any solution or dilution of cocaine or its salts in an inert substance whether liquid or solid, containing any proportion of cocaine, and any preparation, admixture, extract or other substance (not being such a solution or dilution as aforesaid) containing not less than one-tenth per cent. of cocaine or of ecgonine."

Note.—"Ecgonine" is used above to mean lævo-ecgonine, and includes any derivatives of ecgonine from which it may be recovered industrially.

[P1] "Alkaloids, the following; their salts, simple or complex:—Coca, alkaloids of."

"Amino-alcohols, esterified with benzoic acid, phenylacetic acid, phenyl propionic acid, cinnamic acid or the derivatives of these acids."

"Guanidines, the following.—Polymethylene diguanidines, di-para-amylphenetyl guanidine."

"Orthocaine; its salts."

"Oxycinchonic acid, derivatives of; their salts; their esters."

"Para-amino-benzoic acid; esters of; their salts."

"Phenetidylphenacetin."

[81] "Alkaloids, the following; their salts, simple or complex:—Coca, alkaloids of, except substances containing less than 0.1% of the alkaloids of coca."

"Amino-alcohols, esterified with benzoic acid, phenylacetic acid, phenyl propionic acid, cinnamic acid or the derivatives of these acids, except in substances containing less than 10% of esterified amino-alcohols."

"Guanidines, the following.—Polymethylene diguanidines, di-para-amylphenetyl guanidine"

"Oxycinchonic acid, derivatives of, their salts; their esters."

"Phenetidylphenacetin."

Dose.— $\frac{1}{4}$  to 1 drachm (1 to 4 g.).

HISTORY OF COCA. The plant originally named "Khoka," meaning "the tree of trees," first became known in Europe through the writings of Garcilaso Inca de la Vega, a student of Peruvian history, who died in 1616. Joseph de Jussieu in 1750 was the first to send specimens of the plant to Europe.

The dried leaves of *Erythroxylum Coca* (Bolivian or Huanuco Leaf) or of *E. truxillense* (Peruvian or Truxillo leaf) (Erythroxylaceæ).

The Bolivian leaves are browner, larger, broader and thicker; the veins are prominent; and there are clearly defined lines on each side of the midrib, which shows a distinct ridge in its centre.

Those of *E. truxillense* are pale green, less oval and more elliptical in outline, and are much more fragile, being frequently broken.

The Bolivian leaves, imported from that country, are preferred for medicinal use, since a larger proportion of the alkaloids is cocaine. Java supplies most of the Truxillo variety. Ceylon was at one time a regular producer, but cultivation was abandoned at the request of the British Government. Coca is now frequently valued on its ecgonine content since commercial cocaine is obtained synthetically from ecgonine.

The total alkaloid content varies from 0.5 to 1.5%. Truxillo and Java leaf contains more, but only about 50% is cocaine. The total alkaloid of Bolivian leaf contains 70 to 80% of cocaine.

**Uses.** As a nerve and muscle stimulant, and of value in gastralgia, nausea and vomiting, and for the discomfort following excessive eating or drinking. Coca leaf chewing is extensively practised in Bolivia and Peru, 2 to 4 ounces being used per day. It staves off hunger and fatigue and gives stamina.

[P1] **Elixir Cocæ** (B.P.C.) *Dose.*—1 to 4 drachms (4 to 15 ml) in water.

A palatable preparation containing 16½% v/v of liquid extract of coca equivalent to about 0.08% w/v of alkaloids; 4 dr contains about ½ gr.

[D P1 81] **Extractum Cocæ.**

*Dose.*—2 to 15 grains (0.12 to 1 g), in pills or pastilles. A dry extract, made with alcohol 60% and standardised to 2% of alkaloids (1 = about 4 of leaves).

[D-P1-81] **Extractum Cocæ Liquidum** (B P C.). *Syn.* MISCIBLE LIQUID EXTRACT OF COCA.

*Dose.*—½ to 1 drachm (2 to 4 ml). Standardised to contain 0.5% of ether-soluble alkaloids; 1 dr. contains about ½ gr of coca alkaloids.

A single emergency dose of Extractum Cocæ Liquidum said to act "like a charm" in cases of *hæmorrhage due to piles*, when patient has to stand for any length of time.—C. E. Shelley, *Practitioner*, i/1923, 211.

[P1] **Vinum Cocæ.**

Elixir of coca 1, detannated sherry-type wine to 8 *Dose.*—½ to ½ ounce (8 to 15 ml.) diluted with wine or water. Checks vomiting

[D P1 81] **Cocaina** (B.P., F.E. VIII, P. Helv. V, U.S.P. XI) *Syn.* METHYL-BENZOYLECGONINE.  $C_9H_{13}(CH_3)(C_6H_5CO)NO_3 = 303.2$

*Dose.*—½ to ½ grain (0.008 to 0.016 g.), in a pill or tablet

In shining monoclinic prisms, m.p. 97° to 98°. It is obtained from coca, and was first isolated by Niemann in 1860.

**FIRST USE OF COCAINE.** J. H. E. Brock is believed to be the first to use cocaine subcutaneously for surgical purposes at University College Hospital in 1884. For details see Vol. I, 20th Edn., p. 333.

**Soluble** 1 in 10 of alcohol 90%, 2 in 1 of chloroform, about 1 in 4 of ether, 1 in 80 of light petroleum, 1 in 100 to 150 of liquid or soft paraffin, 1 in 10 of castor oil, 1 in 24 of olive oil, 1 in 2 of warm anhydrous wool fat; soluble in oil of clove and other volatile oils Soluble 1 in 1300 of water and about 1 in 1000 of 1% sodium bicarbonate. Insoluble in glycerin.

**Antidotes.** (Acute poisoning.) Emetics will probably be useless, so empty stomach by stomach tube, using dilute solution of potassium permanganate or tannic acid. Give medicinal charcoal stirred up in water. (If the cocaine has been injected, obviously the use of the stomach tube and charcoal is useless.) Keep patient lying down and warm. Ammonia inhalations. Strychnine,  $\frac{1}{2}$  gr hypodermically Sodium Amytal, 3 to 10 ml. of 10% solution, intravenously at rate of 1 ml. per minute, or chloroform, for convulsions Coramine, 5 to 15 ml of 25% solution, intravenously for circulatory collapse.

### **Cocaine Addiction.**

Cocaine fascinates by the rapidity with which it relieves exhaustion and dispels gloom by producing a delightful sense of mental and physical vigour. The habit is not common. News reports concern rather cases of users of the drug for specific purposes than addiction. The discomforts caused by cocaine are readily controlled by morphine and when the patient learns this, the addiction becomes confirmed. Atropine, or better, hyoscine is the best for treatment of addiction of all kinds De Quincey found benefit from valerian.

COCAINE SNIFFED UP THE NOSE is readily absorbed. It first powerfully stimulates the brain and lassitude and fatigue pass, but a marked depression of the central nervous system succeeds. Frequent application to the nose causes perforation of the nasal septum. Abstinence symptoms are less severe than in the case of morphine, and it can be cut off at once.

In cocaine addiction,  $\frac{1}{4}$  grain produces very little effect on an ordinary person,  $1\frac{1}{2}$  grains is usually well tolerated, and the total dose varies between 8 and 23 grains. The action of the drug varies greatly with different individuals and when death results it is due to sudden paralysis of the central nervous system.

**Uses.** For general uses of cocaine and its salts *vide* Cocainæ Hydrochloridum. The base is used for the preparation of oily solutions and ointments. A solution in olive oil has been used to anaesthetise the mucous membrane and allay cough in cauterising laryngeal growths.

A 2% solution in almond oil is mostly used for earache. For the eye a 2% solution in castor oil is used, sometimes combined with homatropine, for catheters, a solution in equal parts of castor and almond oils is useful.

1 or 2% in soft paraffin is suitable for eye work, and 4% or stronger is useful for catheterisation, burns, and for intense sensitiveness of parts, pruritus, etc.

[D·P1·81] **Bugitaria Cocainæ** (B.P.C.) contain  $\frac{1}{2}$  grain of the alkaloid. Useful in urethral affections.

[D·P1·81] **Guttæ Cocainæ** (B.P.C.). *Syn.* COCAINE EYE DROPS (FACTORY ACT, SOLUTION No. 1), FACTORY EYE DROPS.

For a foreign body in the eye.

Dissolve powdered cocaine (base) 0·5 g in castor oil 95 g. on a water bath. While still warm add a solution of 0·033 g. of mercuric chloride in 1 ml. of dehydrated alcohol. Mix by rotating. Apply with a camel hair brush.

On standing, crystals of benzoyl-ecgonine are deposited and it has been suggested that the cocaine should be replaced by 1% of procaine base.

[D P1 81] **Gutt. Cocain. c. Oleo** (N.I.F.).

Cocaine 2 gr., castor oil to 2 dr.

[D P1·81] **Nebula Cocainæ Composita** (B.P.C.) contains 0·5% w/v of cocaine in compound menthol and thymol spray.

[D P1 81] **Nebula Cocainæ Oleosa.**

Cocaine 1, oleic acid 4, liquid paraffin to 20.

[D·P1·81] **Unguentum Cocainæ** (B.P.C.). Cocaine 4%, as oleate, in lard Useful where absorption is required, as in facial neuralgia, shingles, eczema, crysipelas, urticaria, and pruritus.

[D·P1·81] **Cocainæ Hydrochloridum** (B.P., U.S.P. XI, P. *Helv.* V, P. *Dan.*, and in most national Pharmacopœias).  $C_{17}H_{21}O_4N \cdot HCl$  = 339·6.

*Dose.*— $\frac{1}{2}$  to  $\frac{1}{4}$  grain (0·008 to 0·016 g.), but more may be given, in solution, pill or pastille. *Hypodermically*  $\frac{1}{4}$  to  $\frac{1}{2}$  grain (0·016 to 0·03 g.).

*Fr. Cx.* and *P.G. VI* give maximum single dose,  $\frac{3}{4}$  grain; maximum during 24 hours, 2 $\frac{1}{2}$  grains approx. *P. Ital. V* and *P. Helv. V*  $\frac{1}{2}$  and 1 grain respectively.

Shining, lamellar crystals, with bitterish taste One part of cocaine base = 1·12 of the hydrochloride.

**Soluble** 2 in 1 of water, 1 in 3 of alcohol, also in glycerin; insoluble in ether, fats, and oils. It will crystallise with 9·5% of water of crystallisation, but the anhydrous salt is preferred. M. p. when placed in heating bath at 193°, not below 197°.

For a review of investigations into the loss of activity of solutions on keeping, see *Pharm. J.*, ii/1934, 501.

Conflicting results have been reported but it appears to be desirable that the reaction of the solution should be about pH 5 before sterilisation.

**Incompatible** with ammonium carbonate (soluble in excess), phenol, mercuric and mercurous chlorides. It is also precipitated by borax.

When borax and cocaine hydrochloride are prescribed together, a weight of boric acid equal to that of the borax should be ordered at the same time to prevent precipitation.

In dispensing white precipitate with cocaine hydrochloride in the form of an ointment, dissolve the cocaine salt in a drop or two of water Rub the white precipitate down with a little almond oil, mix, and add the remainder of the ointment base—*e.g.*, soft paraffin.

With phenol, cocaine hydrochloride is compatible in presence of glycerin or alcohol, but not in aqueous solutions.—*Pharm. J.*, i/1925, 233; *Chem. & Drugg.*, i/1925, 313.

#### Activity of Different Cocaine Salts.

Solutions of different cocaine salts containing 0.892% *w/v* of cocaine base (= 1% of hydrochloride) were tested on the rabbit's cornea. The following figures give the per cent. concentrations of cocaine hydrochloride which are equivalent to the solutions used.—Citrate 0.2, lactate 0.4, tartrate 0.6, sulphate 0.8, phosphate 1.0, hydrochloride 1.0, hydriodide 1.2, sulphocyanate 1.5, formate 2.5, acetate 2.9, salicylate 4, benzoate 5, phenylacetate 12.—J. Regnier and R. David, *J. Pharm. Chim., Paris*, 1935, 16.

#### Uses of Cocaine and its Salts.

Renders the superficial structure of the eye anæsthetic, is a mydriatic, and paralyses the accommodation. Applied to mucous membrane it blanches the part, simultaneously producing anæsthesia. Application of an ointment (alkaloid) will remove the pain of eczema, erysipelas, facial neuralgia or shingles, and the irritation of urticaria or pruritus.

For burns and scalds, brush with a 4% aqueous solution (hydrochloride) and apply cocaine ointment on cotton wool or lint; for fissured nipples and insect bites, apply an aqueous solution; for hay fever, influenza, coryza, bronchitis, spasmodic asthma, laryngitis and pharyngitis, a spray of an aqueous solution to relieve irritability of mucous surface. Spasmodic and painful affections of the vagina may be minimised by vaginal injections of  $\frac{1}{4}$  grain in 1% oily solution; rectal and prostatic pains are relieved by  $\frac{1}{2}$ -grain suppositories. A rectal injection checks diarrhœa and dysentery.

IN DENTISTRY. For extraction, 1 ml. of 1 to 2% solution is used with the addition of  $\frac{1}{4}$  to 1 minim of solution of adrenaline hydrochloride. For plugging, preparations such as 10% cocaine in lanolin, Calorific Fluid or Cocaine-Menthol-Eugenol are used.

FOR SMALL OPERATIONS. Solutions of cocaine hydrochloride have been used in excision of the tonsils, cauterising the turbinated tissue of the nose, painting chancres previous to the application of caustics, removing polypi, iridectomy and operation for cataract, squint, and the removal of foreign bodies from the eye. For the eye aqueous solutions of cocaine hydrochloride 2 to 4% strength and for other purposes 4 to 50%; it is necessary to repeat the application of the weaker solutions. No operation should be commenced within at least 10 minutes of the first application. Injurious effects, either local or constitutional, rarely follow its use.

FINGER AMPUTATION. Cocaine solution 5%, to which 5 m. of liquefied phenol and 5 m. of solution of adrenaline hydrochloride have been added to each ounce of the solution: never exceeding 90 m., often less.

The nose may be plugged with strips of gauze soaked in 10 to 20% cocaine solution, to which a few drops of 1 in 1000 adrenaline have been added. In the urethra not exceeding 1% should be used, as absorption is rapid.

None of the synthetic local anæsthetics equal cocaine when applied to mucous membrane. Operations should be preceded by



morphine and atropine hypodermically. In nose operations *adrenaline* should be applied followed by cocaine, injection being made slowly.

In throat operations a 5 to 10% solution should be applied first

For ear operations as local anæsthetic. Cocaine hydrochloride, menthol, phenol, clove oil, and rectified spirit, equal parts —F Pearce Sturm, *Brit. med J.*, ii/1926, 638.

**ENUCLEATION OF THE TONSIL** under local anæsthetic For surface anæsthesia a mixture of equal quantities of 10% cocaine hydrochloride solution and adrenaline solution used, applied with cotton swabs, and repeated three or four times, followed by infiltration of the tissues in which the tonsil lies embedded with a 5% Novocain solution —Dan McKenzie, *Prescriber*, May, 1922, 314

Cocaine hydrochloride has been used for *intraspinal anæsthesia* using  $\frac{1}{2}$  to 2% solution, but it is generally considered too toxic for this purpose.

**LOCAL INFILTRATION ANÆSTHESIA** is produced by 0.1 to 0.2% solutions of cocaine with a small quantity of adrenaline solution. Its action commences in three minutes, increases for ten to twenty minutes, and mostly disappears within half an hour. The anæsthesia may be prolonged by applying a triangular bandage when possible above the site of injection; this has also the advantage of lessening the risk of toxic symptoms, as the delay of cocaine in the tissues renders it innocuous.

[D P1-81] **Auricular Cocainæ Hydrochloridi.** Ear cones, contain  $\frac{1}{8}$  gr in each with oil of theobroma basis.

[D P1-81] **Guttæ Cocainæ (R L O H)** Cocaine hydrochloride 8 or 16 gr to 1 oz.

[D P1-81] **Guttæ Cocainæ cum Adrenalina.**

Cocaine hydrochloride 5% in solution of adrenaline hydrochloride

[D P1-81] **Injectio Cocainæ et Sodii Bicarbonatis.** Cocaine hydrochloride  $\frac{1}{2}$ , sodium bicarbonate  $\frac{1}{2}$ , chlorbutol  $\frac{1}{2}$ , distilled water to 100

*Dose.*—2 to 4 drachms (8 to 15 ml.) for *urethral injection*

This solution is remarkably efficacious for use prior to passing a catheter

[D P1-81] **Lamellæ Cocainæ (B P.).** DISCS OF COCAINE

Discs of gelatin, each containing  $\frac{1}{8}$  gr. of cocaine hydrochloride, are for ophthalmic use. Also prepared containing  $\frac{1}{8}$  gr in each in combination with atropine sulphate (q v), and homatropine (q v)

[D P1-81] **Isotonic Cocaine Eye Lotion.**

Cocaine hydrochloride 1, sodium chloride 1.25, distilled water to 100. This is isotonic with the tears

[D P1-81] **Nebula Cocainæ Composita.** Cocaine 2 gr, cinnamon oil 5 m, menthol 15 gr, liquid paraffin to 1 oz

[D P1-81] **Nebula Cocainæ Hydrochloridi.** May be prepared 1, 5 or 10%, or more if ordered, with sterile normal saline for general use

[D P1-81] **Oculentum Cocainæ (B P)** contains 0.25% of cocaine hydrochloride.

[P1] **Pastilli Cocainæ Hydrochloridi (B P C)** contain  $\frac{1}{8}$  gr (0.0016 g)

To allay throat irritation and hoarseness

[D P1-81] **Pigmentum Cocainæ et Hydrargyri Perchloridi.** Cocaine hydrochloride 28 gr, solution of mercuric chloride 20 drops, glycerin 4 dr, water 4 dr, after syringing ears twice or thrice daily with boric acid lotion

Of value for painting the external auditory meatus and membrana tympani

[D P1-81] **Solutio Bonain (T.H)** Phenol, menthol and cocaine hydrochloride, equal parts.

[D P1 81] **"Cocaine-Menthol-Eugenol."** Cocaine, menthol, eugenol and alcohol 90% equal parts. Applied on a pledget of cotton wool, followed by jets of cold air, *e g*, from a chip syringe, relieves toothache rapidly

[D P1 81] Camphor 5, chloral hydrate 5, cocaine hydrochloride 1, warmed, form an oily liquid which cures toothache

[D P1 81] **Suppositories and Pessaries**  $\frac{1}{2}$  grain (0.03 g), or more *SH* 1926 has Pessus 1 grain in 2 drachms

[D P1 81] **Compound Cocaine Suppository** of cocaine hydrochloride  $\frac{1}{8}$  gr with morphine hydrochloride  $\frac{1}{2}$  gr is useful for painful hæmorrhoids

[D P1 81] **Tabellæ Cocainæ.**  $\frac{1}{8}$ ,  $\frac{1}{16}$ , and  $\frac{1}{32}$  grain with chocolate The usual dose is  $\frac{1}{8}$  grain.

*Dose.*—1 every quarter, half-hour or hour, quickly eaten and swallowed Useful for sea-sickness, chloroform or alcoholic sickness, and that of pregnancy

Sea-sickness may be overcome by internal use of the following—Cocaine hydrochloride 0.2 g, iodine tincture 2 ml, water to 150 ml *Dose*—1 table-spoonful 2 to 4 times daily More palatable without the iodine.

[D P1 81] **Trochisci Cocainæ Hydrochloridi** (*TH*)  $\frac{1}{16}$  grain (0.005 g) in each *Brompton H* has  $\frac{1}{8}$  grain in 20 grains

[D P1 81] **Codrenine** (*Parke, Davis, London*) Cocaine hydrochloride 2% and adrenaline chloride 1 in 15,000. *Dose*—For dental extractions 8 minims. Local anæsthetic.

[D P1 81] **Dental Anæsthetic** (*Martindale, London*) Solution containing 0.85% of cocaine in combination with iodine and hæmostatics

[D P1 81] **Locosthetic** (*Parke, Davis, London*) Cocaine hydrochloride 0.75% with adrenaline chloride 1 in 50,000 Analgesic for use in dentistry. Locosthetic Modified is similar with 1 in 100,000 of adrenaline chloride

[D P1 81] **Cocainæ Nitras** (*PG VI, P Helv. V*)



*Dose*— $\frac{1}{16}$  to  $\frac{1}{8}$  grain (0.008 to 0.016 g.).

In large colourless crystals, readily soluble in water Is compatible with silver nitrate, and if used previously in solution lessens the pain caused by the latter salt.

[D P1 81] **Cocaine Periodide.**  $\text{C}_{17}\text{H}_{21}\text{O}_4\text{NI}_3 = 684.1.$

*Dose.*— $\frac{1}{16}$  to  $\frac{1}{8}$  grain (0.0015 to 0.003 g) increased with care, in a cachet

In dark purple crystals containing 44.3% of cocaine. Insoluble in water and ether, nearly insoluble in chloroform, slightly soluble in alcohol 90% Is stable in physiological acid, but decomposed by alkalis Has been suggested for relief of painful affections of the bowels.

[D P1 81] **Cocainæ Phenas.** *Syn* COCAINE CARBOLATF

*Dose.*—In pill  $\frac{1}{16}$  to  $\frac{1}{8}$  grain (0.003 to 0.03 g).

A slightly soluble pasty compound, used by dentists and given for gastralgia Is strongly antiseptic and may be used on cut surfaces, as its coagulating effect on albumen prevents too rapid action.

[D P1 81] **Cocainæ Salicylas.**  $\text{C}_{17}\text{H}_{21}\text{O}_4\text{N}, \text{C}_6\text{H}_4(\text{OH})\text{COOH} = 441.2.$  *Dose.*— $\frac{1}{16}$  to  $\frac{1}{8}$  grain (0.008 to 0.016 g)

In white deliquescent masses; it forms a solution which keeps well. Soluble 5 in 1 of water,  $2\frac{1}{2}$  in 1 of alcohol 90%. In spasmodic asthma, the hypodermic injection of a full dose at the beginning relieves the attack.

[D.P. 81] **Palcaine** (*Merck, Darmstadt; Martindale, London*). The acid tartrate of *d*-pseudo-cocaine, a synthetic isomer of cocaine. A white powder, soluble in 4 of water, yielding a faintly acid solution.

Both Psicaine and cocaine give rise to symptoms identical in character, though not in degree; Psicaine is the more powerful stimulant. Irritant effect less than cocaine and insignificant for practical purposes. It has relatively little effect on blood vessels. It was found to be more toxic and less efficient than cocaine.—A. J. Copeland, *Brit. med. J.*, i/1925, 10

[P. 81] **Tropacocainæ Hydrochloridum** (*P.G. VI*). *Syn.* BENZOYL PSEUDOTROPINE HYDROCHLORIDE.



The salt of the base tropacocaine obtained from Java coca, or synthetically. In white crystals, m.p.  $271^\circ$ . Freely soluble in water. Is a powerful anæsthetic; in the eye causes neither ischæmia nor irritation of hyperæmia. 3% solution recommended; anæsthesia is produced more quickly than with cocaine but is more transitory; the action may be kept up by adding a drop from time to time. Mydriasis occurs occasionally but is slight. Injection into gums in large doses only affected pulse for 10 minutes and did not affect respiration. Aqueous solutions keep well and can be boiled with impunity. Severe sciatica has been treated successfully by injecting 1 ml. of 5% solution into the dural sac in the lumbar region.

The 5% solution has been used for intraspinal anæsthesia, the dose for a healthy person weighing 11 stones being 20 m., a further 8 to 12 m. being given 40 to 50 minutes later if required.

**Erythrophloeum.** *Syn.* CASCA BARK, SASSY BARK, ORDEAL BARK. The bark of *Erythrophloeum guineense* (*Leguminosæ*). Contains the alkaloid erythrophloeine which has a digitalis action and is also anæsthetic.

**Tinctura Erythrophloei.** 1 in 10 of alcohol 90% *Dose*—5 to 10 minims.

**Erythrophloeinæ Sulphas.** *Dose.*— $\frac{1}{10}$  to  $\frac{1}{2}$  grain in pill. Yellowish granular crystals, very soluble in water. Has the combined action of digitalin and picrotoxin, and is a local anæsthetic for eye work in 0.05 to 0.25% solution, also as a dental obtundent in 50% solution in eugenol.

[P. 81] **Amydricainæ Hydrochloridum** (*B.P.C.*). *Syn. and Prop. Name.* BENZOYL TETRAMETHYLDIAMINODIMETHYLETHYL CARBINOL HYDROCHLORIDE (*P.G. VI*), ALYPIN (*Bayer Products, London*).  $C_6H_5 \cdot COOC(C_2H_5)[CH_2N(CH_3)_2]_2 = 314 \cdot 7$ .

*Dose.*— $\frac{1}{10}$  to  $\frac{1}{2}$  grain (0.003 to 0.03 g.) *per os*.

White, crystalline powder melting at about  $169^\circ$ . Soluble 1 in 1 of water and 1 in 4 of alcohol 90%.

Solutions containing 0.025 to 0.5% or up to 10% are efficient in eye work. (Strong solutions keep well, but weak ones may become cloudy; they may be sterilised by boiling). 2% strength produces insensibility of cornea in sixty seconds. Non-toxic, it produces no mydriasis nor any disturbance of accommodation.

For lumbar anæsthesia injection of  $\frac{1}{2}$  to 1 ml. of 2% solution has been used. For infiltration 0.01 to 0.1% solution has been used with same quantities of cocaine hydrochloride in 0.2% sodium chloride solution.

Internally in sickness and post-operative vomiting it acts like cocaine.

[P1 81] **Amylocainæ Hydrochloridum** (B P., P. Ital. V, P. Belg. IV, P. Argent. II, F.E. VIII). *Syn. and Prop. Name.* CHLORHYDRATE D'AMYLÉINE (Fr. Cx. Supp., 1920), STOVAINE (Pharmaceutical Specialities (May & Baker) Ltd., London).

$C_6H_5 \cdot CO_2 \cdot C(CH_3)(C_2H_5) \cdot CH_2N(CH_3)_2 \cdot HCl = 271.6$ .

*Dose.*—Per os and hypodermically,  $\frac{1}{2}$  to  $\frac{3}{4}$  gr. (0.02 to 0.05 g.). By intrathecal injection,  $\frac{1}{2}$  to  $1\frac{1}{2}$  grain (0.02 to 0.1 g.). Fr. Cx. Supp., 1920, has maximum single dose  $1\frac{1}{2}$  gr. approx., maximum in 24 hours  $2\frac{1}{2}$  gr. approx. P. Belg. IV gives 5 and 10 gr. approx. respectively.

In small white crystals, melting at  $177^\circ$  to  $179^\circ$ . Consists of the hydrochloride of the benzoyl ester of methylethyldimethylamino-methylcarbinol. Soluble 1 in 2 of water, 1 in 3 of dehydrated alcohol; almost insoluble in ether.

*Uses.* Anæsthetic, vasodilating, comparatively non-toxic. It is stated not to cause headaches, nausea, vertigo, or syncope. Is used in 2 to 4% solution for application to the eye. For turbinal operations and for operations on the ear 5% is used. For hypodermic use,  $\frac{1}{2}$  to 2%. Internally it has been given to allay persistent vomiting.

**ANGINA PECTORIS** Injection of 10 ml of 1% Stovaine solution under the skin at the site of the most severe pain gave definite relief, when nitrites, etc., had failed. Valuable in patients with angina pectoris due to coronary spasm.—*Brit. med. J. Ept*, 11/1931, 7.

[P1] **Amylocaine Ointment** for painful wounds and hæmorrhoids:—Amylocaine hydrochloride 0.7, adrenaline solution 20, paraffin ointment 100.

[P1] **Unguentum Adrenalinæ et Amylocainæ Compositum** (B P.C.).

Adrenaline 1–14,000, amylocaine hydrochloride and benzocaine 1% with liquid extract of hamamelis in wool fat and yellow soft paraffin. A valuable soothing ointment for hæmorrhoids.

**Intraspinal Anæsthesia with Amylocaine Hydrochloride.**

The advantages of intraspinal anæsthesia are absence of post-operative shock, complete muscular relaxation, no venous engorgements or respiratory movements, no starvation, and no post-operative sickness. It is contraindicated in cases of advanced sepsis.

The canal is punctured between the second and third lumbar interspaces, the patient being in a sitting posture. 5 ml of fluid is allowed to escape and then the injection made. Anæsthesia is produced within ten minutes, and lasts for about an hour.

By carefully adjusting the curves of the spine, either a high or low anæsthesia can be produced by gravitation. The lowering of the head in any operation is not favoured. The best results are obtained by not altering the level of the body after injection, except in cases of the labouring class advanced in life, where the spinal column may be almost rigid—here the pelvis may have to be raised. Usually 5 to 10 ml. of cerebrospinal fluid is withdrawn

before injection. Any alteration of posture may be made providing the relative levels of head and pelvis remain as before.

To prevent shock following intraspinal anæsthesia, after removal of 5 to 10 ml. of spinal fluid and the injection of the anæsthetic, the spinal fluid is injected intravenously at the bend of the elbow and the operation commenced 5 or 6 minutes later.—*Brit med J Ept.*, 1/1927, 21.

The ideal solution for anæsthesia should produce neither shrinking nor swelling of the blood or tissue cells by osmosis

[P1] **Barker's Solution.** Stovaine 0.1 g, dextrose 0.1 g, water to 2 ml Sp gr. 1.025. *Dose*—1 ml Often the dose may be reduced to 0.8 ml, sometimes increased to 1.2 ml.

Using this solution, a small dose of the drug can be employed and the severest operations performed. The equivalent of 0.06 g. of Stovaine is usually found to be sufficient. As a rule anæsthesia is established in 5 to 7 minutes for the groins and 8 to 10 for the epigastrium. There is almost always pyrexia but no post-operative shock. Highest analgesia—clavicles.

Caffeine, 2 gr. hypodermically, should be given as soon as Stovaine has been administered, to counteract the fall in blood pressure, a second dose should be kept ready in case of emergency (the two "danger periods" are immediately after injection and 20 minutes later) pituitary extract a satisfactory substitute. Let the maximal dose of Stovaine solution be 0.8 ml.—Hamilton Bailey, *Practitioner*, 1/1927, 372.

Other solutions used are the following—

[P1] **Solutio Stovainæ et Glucosi (St. T.H.)** contains 2½ or 5% with dextrose (anhydrous) 2½ or 5%

[P1 81] **Chaput's Solution.** *Syn* 'TUFFIER'S SOLUTION (M.R.I.) Stovaine 0.1 g, sodium chloride 0.1 g, water to 1 ml. Sp. gr. 1.080.

[P1] **Kroenig's Solution (M.R.I.)** Stovaine 0.08 g, sodium chloride 0.0022 g, water to 2 ml

[P1] **Chaput's Alcohol Solution (M.R.I.)** Stovaine 0.08 g, alcohol 95%, 0.2 ml, water to 2 ml.

Stovaine-saline solutions give good results but a number of patients would prefer to sleep.—R. B. Coleman, *Brit med J*, 1/1925, 548.

These solutions are sometimes preferred because they diffuse more readily than the solution containing dextrose.

[P1] **Jonnesco's Stovaine Caffeine Solution** contains from 0.02 to 0.05 or 0.1 g of Stovaine with caffeine 0.5 g and sodium benzoate—*Vide Pr méd*, Oct., 1922, 929.

[P1] **Duplas' Solution (M.R.I.)** Stovaine 0.06 g, caffeine 0.1 g, sodium benzoate 0.1 g, water to 2 ml

Caffeine is included in these formulæ to counteract the fall in blood pressure, and is preferred to strychnine, which was at one time advocated for the purpose by Jonnesco.

Favourable results in spinal anæsthesia with Stovaine and caffeine.—B. Desplas, *Lancet*, 11/1923, 1235.

### Combined Spinal and Splanchnic Anæsthesia.

For abdominal operation in the neighbourhood of the diaphragm, spinal anæsthesia with 0.1 g. of Stovaine (between the second and third lumbar vertebræ), combined with splanchnic anæsthesia with 60 to 70 ml. 0.5% solution of Novocain, given according to Braun's method, is the anæsthetic of choice. In operations lasting over an hour spinal anæsthesia alone is not sufficient. Anæsthesia may be prolonged by a further dose of splanchnic anæsthetic and infiltrating the peritoneal and abdominal muscles with 0.5% Novocain in 1 in 200,000 adrenaline solution. In nervous patients,

a dose of Avertin per rectum produces quiet sleep. The combination gives complete and uniform muscular relaxation and reduces diaphragmatic movements to a minimum. The method gave a 50% fall in mortality from abdominal operations—B Hughes, *Brit med J.*, 1/1929, 898.

[P1 81] **Benzamina Hydrochloridum** (B.P.C.) *Syn and Prop.* Name. BETACAINE, BETA-EUCAINE HYDROCHLORIDE (*Schering, London*), EUCAINE HYDROCHLORIDE (*U.S.P. XI*), 4-BENZOYLOXY-2:2-6-TRIMETHYLPYPERIDINE HYDROCHLORIDE

$C_{15}H_{17}N(CH_3)_3(C_6H_5COO),HCl = 283.6$

Dose —  $\frac{1}{8}$  to  $\frac{1}{2}$  grain (0.008 to 0.03 g.) or more.

A white crystalline synthetic compound allied to cocaine, *soluble* about 1 in 30 of water (crystals may deposit on cooling but can be redissolved without harming the salt), 1 in 35 of alcohol 90% and 1 in 6 of chloroform at 25°. 2% solutions are used in ophthalmic work. Solutions may be boiled without decomposing the salt.

**Local Infiltration Anæsthesia** (*Barker*) with benzamine hydrochloride is suitable for very short operations using a solution of benzamine hydrochloride 3 gr. (0.2 g.), sodium chloride 12 gr. (0.8 g.), and water to 3½ oz. (100 ml.). This is isotonic.

The solution is boiled and on cooling 10 m of adrenaline solution may be added. In the operation 50 ml or more (up to 100 ml) is injected all round the region to be dealt with.

[P1] **Nebula Benzaminæ.**

Benzamine hydrochloride 10 gr., sodium sulphate 4 gr., distilled water to 1 oz.

[P1] **Pastilli Benzaminæ** (B.P.C.) contain  $\frac{1}{4}$  gr (0.03 g.)

[P1] **Unguentum Benzaminæ.**

Benzamine hydrochloride 1, olive oil 2, hydrous wool fat 7. For pruritus, menthol 2% may be added.

[P1 81] **Beta-Borocaine** (*British Drug Houses, London*) Benzamine borate,  $C_{15}H_{19}O_3N,5HBO_3$ . Dose —  $\frac{1}{4}$  grain (0.025 g.) A surface anæsthetic. Borocaine is preferred for injection.

For operative work on the eye, a 0.25% solution is recommended, and for operations on and examinations of the urethra and bladder in general a 0.5% solution is suitable.

It has three times the anæsthetic action on the rabbit's cornea, and  $\frac{1}{10}$  the experimental toxicity of cocaine hydrochloride. It is mildly irritant, causes some congestion, especially in the nose, and in very large doses excites the central nervous system—A. J. Copeland, *Brit med J.*, 1/1926, 82.

[P1 81] **Beta-Borocaine Tablets** contain 0.025 g., with adrenaline 0.00005 g., sodium chloride and cane sugar *q.s.* One dissolved in 10 ml makes a 0.25% solution. 1 in 5 ml makes a 0.5% solution.

[P1 81] **Benzaminæ Lactas** (B.P.C.). *Syn* EUCAINE LACTATE, BETACAINE LACTATE  $C_{15}H_{21}O_3N, C_3H_5O_3 = 337.2$ .

Dose —  $\frac{1}{8}$  to  $\frac{1}{2}$  grain (0.008 to 0.03 g.).

A white crystalline salt with m.p. 152° to 156°.

**Soluble** about 1 in 5 of water and about 1 in 8 alcohol (90%).

**Incompatible** with salicylic acid.

For ophthalmic work and in dentistry employ 2 to 3%, for infiltration 0.1% with sodium chloride 0.8%; for regional anæsthesia 2.5%; nose, throat and ear 10 to 15%; for urethral injection, 1 to 2% solutions may be used to relieve pain. Solutions can be boiled.

It is slower in action than cocaine, is less toxic, and anæsthesia is more prolonged, while the heart is not affected, nor the pupil dilated.

Sciatica has been treated by injections.

[P1] **Benzocaina** (B.P.). *Syn. and Prop. Name.* ETHYL *p*-AMINO-BENZOATE (U.S.P. XI, P.G. VI, P. Helv. V, P. Dan., P. Ned. V, F.E. VIII, P. Belg. IV), ANÆSTHESIN (Bayer Products, London).  $\text{NH}_2 \cdot \text{C}_6\text{H}_4 \cdot \text{CO}_2 \cdot \text{C}_2\text{H}_5 = 165 \cdot 1$ .

*Dose.*—5 to 10 grains (0·3 to 0·6 g.) in powder or cachets. U.S.P. XI average dose 5 grains.

White crystalline powder, m.p. 90° to 91°, with slightly bitter, numbing taste.

**Soluble** 1 in about 2500 of water, 1 in 8 of alcohol 90%, 1 in 4 of ether, 1 in 2 of chloroform, 1 in 50 of almond oil, 1 in 35 of olive oil.

**Uses.** To relieve hyperæsthesia of the stomach and dyspepsia: local insufflations sometimes with equal amount of orthocaine for pharyngeal and laryngeal affections; bougies 3 grains for urethritis, and suppositories 10 grains for hæmorrhoids. Ointments 10% for burns, eczema and intertrigo.

Pneumococcic (and tuberculous) infection of the throat, in a case of difficulty in swallowing, has been greatly relieved by applications of benzocaine dissolved in palm oil—in form of a spray

Great relief of pain in inoperable carcinoma of the rectum from suppositories of benzocaine 5 gr. and acetylsalicylic acid 10 gr—D G Greenfield, *Brit med. J.*, ii/1932, 1041.

### [P1] "A.B.A."

Benzocaine 3, benzyl alcohol 5, and ether 10, in sterile olive oil q.s. to 100.

In PRURITUS ANI 10 ml. may be safely used at the first treatment—injected in relation to the posterior half of the perianal region through 4 punctures, 2½ ml. at each point. A week later 5 ml. is given by 2 punctures, and again another dose after a further week. In the average case, 3 doses—10, 5, and 5 ml.—suffice

Permanent relief of pruritus ani from subcutaneous injections (round the anal margin) of either Benacol—a solution of equal parts of benzocaine and benzyl alcohol in 90 parts of almond oil, or A.B.A. as above. 4 ml. of either may be injected at a time and repeated at 3 to 7-day intervals, till the entire perianal region has been injected, 8 ml. being the average total injected. No general reaction or complications. Also gives rapid and brilliant cure in recent anal fissure.—W. B. Gabriel, *Brit. med. J.*, i/1929, 1071

A.B.A. valuable for ano-rectal complaints—better than Novocain—P. Kennedy Murphy, *Brit. med. J.*, ii/1930, 162

Large doses of both oily and aqueous solutions as anæsthetics in pain and fissure should be avoided.—P. Kennedy Murphy, *Brit. med. J.*, ii/1930, 498

Anal fissure treated by 2 to 5 ml. of A.B.A. injections into the sphincter.—W. J. Lytle, *Brit. med. J.*, i/1931, 498.

Pruritus ani and anal fissure, and spasm of the sphincters, treated by A.B.A. Pain relieved instantly.—Arthur S. Morley, *Brit. med. J.*, ii/1930, 80.

Percaine (see p 401) 0·5%, benzyl alcohol 10%, phenol 1%, in 5 ml. of sterile oil, also used instead of the above. For anal fissure A.B.A. 5 ml., or the Percaine in oil (5 ml.) will reduce sphincteric relaxation. Local anæsthetic effect lasts as long as 10 days.—W. B. Gabriel, *Brit. med. J.*, ii/1930, 311.

Percaine in oil (made up according to Gabriel's formula) is the most satisfactory local anæsthetic in hæmorrhoidectomies; anæsthesia lasts from 7 to 10 days. Contraindications are local infection, eczema and a possible idiosyncrasy. —N. J. Simmons, *New Engl. J. Med.*, 1936, 214, 20.

**RECTAL ANÆSTHESIA.** A.B.A. and the Percaine solution both found to give rise to pain on injection and very often to severe pain several hours afterwards. The following formula is an improvement. Procaine base 1.5%, butyl-para-aminobenzoate 6%, benzyl alcohol 5%, in sterilised almond oil. Its advantages are its certainty of effect, painlessness on injection (if given slowly), freedom from severe after-pain, anæsthesia or hypoæsthesia produced for periods up to 28 days or longer. It is comparatively non-toxic, 20 to 30 ml may be injected without ill-effect and with no local reaction. The solution, first warmed, is injected into the deeper tissues at the inner boundary of the ischio-rectal fossæ as well as into the more subcutaneous plane. On no account should an injection be given in the presence of acute sepsis, and when there are excoriations the needle must be inserted through clean normal skin. Good results in the treatment of fissure-in-ano (5 to 10 ml average amount injected) and pruritus ani (from 15 to 30 ml injected at one time). —C. N. Morgan, *Brit. med. J.*, 11/1935, 938.

**PRURITUS VULVÆ.** Though A.B.A. does not cure the condition, it affords a long relief, enabling septic scratches to heal and the patient to gain much-needed rest. —A. Bourne, *Practitioner*, 11/1933, 441.

Of 15 patients treated 5 were cured, 5 much improved, 4 slightly improved and 1 not improved. Weekly injections of 2 ml just beneath the skin in such manner that a fan-shaped area is treated, a different zone being dealt with at each visit, until eventually the whole vulvar region has been infiltrated. The number of injections varied from 3 to 33. —C. W. Kennedy, *Edinb. med. J.*, Sept., 1933, 125.

[P1] **Steriles B.A.B.A.N.** (*Martindale, London*) contain 5 ml. of an alcohol-oil solution of Butesin and benzocaine with 1% of procaine base.

The addition of 1% of basic Novocain as in B.A.B.A.N., is a distinct improvement, a more immediate effect is noted after its injection, and also an excellent late anæsthetic effect is developed, pain after injection is usually absent. In anal spasm and fissure the deep injection of 5, or sometimes 10 ml., of A.B.A. or B.A.B.A.N. into the external fissure has proved of great value. In acute anal fissures a preliminary injection, from a posterior puncture, of 10 ml. of Novocain into the sphincter, on each side of the middle line, is often helpful. In pruritus ani, if palliative treatment fails to relieve the irritation, and in the absence of any local cause, subcutaneous injections of A.B.A. or B.A.B.A.N. are of value, giving 3 injections of 10 ml. at 5 to 7 day intervals. These injections should not be given in the presence of an acute moist dermatitis, and good results are unlikely if the pruritus extends forward to the vulva. —W. B. Gabriel, *Practitioner*, 11/1934, 497.

[P1] **Pigmentum Benzocainæ cum Menthol** (*Brompton H.*).

Menthol 24 gr., acacia 2½ dr., almond oil 2½ dr., water 2½ dr., emulsify, and add benzocaine 90 gr., alcohol 90% 10 dr., water 2 oz.

Painted on the larynx affords relief in tuberculosis of the larynx. —Sir James Dundas Grant, *Practitioner*, 11/1931, 260.

[P1 S1] **Anesthone Cream** (*Parke, Davis, London*) Benzocaine, adrenaline chloride and ephedrine hydrochloride in lanolin and soft paraffin base. Anæsthetic and astringent; gives relief in hay fever and is a palliative in allaying irritation, congestion and inflammation of the nasal mucous membrane.

[P1] **Cycloform Ointment** (*Bayer Products, London*) Alkyl ester of para-aminobenzoic acid 10%, with extract of hamamelis and zinc oxide. Analgesic, antiseptic and astringent; for hæmorrhoids, pruritus, burns, eczema, etc.

[P1] **Proctocaine** (*Allen & Cooper, London*). Procaine base 1.5%, butyl-para-aminobenzoate 6%, benzyl alcohol 5%, in sterilised almond oil. *Dose*.—1 to 5 ml. repeated if necessary at intervals of a week or more. For rectal anæsthesia in anal fissure, pruritus ani, etc.

[P1] **Rhinoculin Cream, Powder and Spray** (*Ritsert, Frankfurt*) contain benzocaine, paranephryn, subcutin, glycerin and boric acid, for use in hay fever.

[P1] **Risin** (*Coates & Cooper, London*). Ointment containing benzocaine, adrenaline, menthol, eucalyptol, boric acid, and soft paraffin and wool-fat. Catarrh, hay fever, etc.



[P1] **Thyngol Pastilles** (*Thilo, Mainz, Coates & Cooper, London*) Each pastille contains benzocaine 0.03 g., phenacetin 0.08 g., thymol, menthol and eucalyptus oil of each 0.0015 g. *Dose*—1 or 2 pastilles per hour, or 10 a day Coughs, dysphagia, etc.

[P1] **Orthocaina** (*B.P., P. Helv V*). *Syn. and Prop. Name* AMINO BENZ, ORTHOFORM (*Bayer Products, London*), METHYL *m*-AMINO-*p*-HYDROXYBENZOATE

$\text{HO} \cdot \text{C}_6\text{H}_3(\text{NH}_2)\text{CO}_2 \cdot \text{CH}_3$   $[\text{HO} \cdot \text{NH}_2 \cdot \text{CO}_2 \text{CH}_3 : 4 : 3 : 1] = 167.1$ .

*Dose*.— $1\frac{1}{2}$  to 3 grains (0.1 to 0.2 g.) for stomach ulceration *P. Helv. V* has max single dose 15 grains, max in 24 hours 45 grains

A white crystalline powder, possessing local analgesic and antiseptic properties.

**Soluble** 1 in 7 of alcohol 90%, 1 in 50 of ether, readily soluble in sodium hydroxide solution, sparingly soluble in water

The [P1] **Hydrochloride**,  $\text{HO} \cdot \text{C}_6\text{H}_3(\text{NH}_2)\text{CO}_2 \text{CH}_3, \text{HCl} = 203.5$ , is soluble about 1 in 9 of water, giving a strongly acid solution The action of the base is more prolonged

A 10% aqueous solution of the hydrochloride, or 10 to 20% with lanolin or paraffin ointment, or collodion solution of pure orthocaine, or this as a dusting powder, may be employed to alleviate pain in sores or burns, but has little action unless the surface is broken.

Has relieved whooping-cough and laryngeal tuberculosis by insufflation.

Eruption following application of 10% orthocaine ointment to septic ulcers of the foot—P. C. P. Ingram, *Brit J Dermat.*, 1933, 526

[P1 81] **Phenacainæ Hydrochloridum** (*U S P XI*) *Syn and Prop. Name*. PHENETIDYLPHENACETIN HYDROCHLORIDE, HOLOCAIN HYDROCHLORIDE (*Bayer Products, London*)

$\text{CH}_3\text{C} \begin{smallmatrix} \text{N} \text{C}_6\text{H}_4 \text{OC}_2\text{H}_5 \\ \text{NH} \text{C}_6\text{H}_4 \cdot \text{OC}_2\text{H}_5 \end{smallmatrix} \text{HCl}, 2\text{H}_2\text{O} = 352.7$ .

The hydrochloride of ethenyl-*p*-diethoxydiphenylamine in small colourless shining crystals

**Soluble** 1 in 55 of water **Incompatible** with alkalis

As an anæsthetic in ophthalmology, 2 to 5 eye drops of 1% solution. It is not adapted for hypodermic use.

[P1 81] **Guttæ Holocainæ** (*R L O H*) Holocain hydrochloride 4 gr. to 1 oz of sterilised water.

[P1 81] **Procainæ Hydrochloridum** (*B.P., U S P. XI, P. Helv V, P. Dan.*).  $\text{NH}_2 \cdot \text{C}_6\text{H}_4 \cdot \text{CO}_2 \cdot \text{C}_2\text{H}_4\text{N}(\text{C}_2\text{H}_5)_2, \text{HCl} = 272.6$  *Syn and Prop. Names*. ETHOCAINE HYDROCHLORIDE (*F.E. VIII*), *p*-AMINO BENZOYLDIETHYLAMINOETHANOL HYDROCHLORIDE (*Fr Cx Supp.* 1920, *P. Ital. V, P. Jap. IV, P. Argent. II, P G. VI, P. Ned V, P. Svec. X, P. Belg. IV*), ALLOCAINE, SYNCAINE, ÆTHOCAINE (*Nederlandsche Cocainefabriek, Amsterdam; Greef, London*), KEROCAIN (*Kerfoot, Bardsley*), NEOCAINE (*Corbière, Paris, Anglo-French Drug Co., London*), NOVOCAIN (*Bayer-Meister Lucius, Leverkusen; Saccharin Corporation, London*), PLANOCAINE (*Pharmaceutical Specialties (Murray & Baker) Ltd., London*)

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regarded as a life-saving measure in the surgery of the old and feeble, and those with cardiac, renal, or pulmonary disease, or diabetes.—Stanford Cade, *Lancet*, i/1925, 856.

Of particular value for operations on the thyroid and thorax.—*Lancet*, i/1925, 879.

**Spinal anaesthesia** with procaine hydrochloride should be reserved for adults, and should not be used in the tuberculous, the syphilitic, or in nervous cases. Specially suitable for operations below the umbilicus.—Brissot (Paris), per *Prescriber*, 1929, 219.

High spinal anaesthesia with injection of 1 ml. of 15% procaine hydrochloride mixed with 8 ml. of the patient's cerebrospinal fluid. After turning patient over, 50 mg. of ephedrine is given hypodermically. In 10 minutes surgeon may commence—he must complete in an hour. Need of a drug to prolong anaesthesia.—C. A. Pannett, *Lancet*, i/1929, 1195. 2% procaine hydrochloride in 0.9% sodium chloride with 1 in 10,000 of adrenaline good for plastic operations of 2 to 3 hours.—C. Abbott-Brown, *Lancet*, i/1929, 1278. Adrenaline should not be used intradurally.—C. A. Pannett, *ibid.*, 1332.

Spinal analgesia with procaine hydrochloride the anaesthetic of choice at the Mayo Clinic for almost all abdominal operations.—I. W. Magill, *Lancet*, i/1931, 353.

Barker's method of Stovaine-Glucose is not used so much now. Procaine hydrochloride is the least toxic of known local anaesthetics. Raising blood pressure by ephedrine injection simultaneously leads to rapid absorption and diminishes the anaesthetic effect. High spinal anaesthesia has many advantages (using 1 to 1.2 ml. of 10% procaine hydrochloride), and is safe if careful technique followed.—C. A. Pannett, *Lancet*, i/1929, 271, 291, see also W. Howard Jones, *Lancet*, i/1929, 362, and reply, *ibid.*, 416.

Planocaine, ethocaine and Novocain in spinal anaesthesia.—*Brit. med. J.*, i/1930, 1154, ii/1930, 43.

Deaths under spinal anaesthesia.—*J. Amer. med. Ass.*, ii/1930, 234; *Lancet*, ii/1930, 650.

In a series of 812 cases (inhalation anaesthesia 474, spinal anaesthesia 338) post-operative complications were 4.29 times more frequent after spinal than after inhalation anaesthesia, in spite of the fact that more "bad risk" patients were operated on under the latter.—A. L. Brown and M. W. Debenham, *J. Amer. med. Ass.*, ii/1932, 210.

As remedial measures for the circulatory depression of spinal anaesthesia are recommended: the raising of the lower part of the body, but not the lowering of the head; the inhalation of oxygen, and the inhalation of dilute ammonia. The injection of ephedrine or adrenaline is not recommended.—C. A. Pannett, *Lancet*, ii/1933, 169.

**Splanchnic analgesia** with procaine hydrochloride. Advantages are perfect relaxation of the abdominal wall with less shock and fatigue to patient. Disadvantages are the extra 15 minutes' time to anaesthetise patient, and in some cases post-operative headache and backache. Operations may be performed which would not be attempted under general anaesthesia alone.

**UPPER ABDOMINAL SURGERY.** Braun's technique modified. The vertebral column between aorta and inferior vena cava is felt just above the pancreas with the left index finger through the lesser omentum. The finger is kept close to the right side of the aorta and the narrow tubular guide of the long fine needle passed along its dorsum down to the vertebra and kept there by the middle finger. The needle is then passed down the guide as far as the bone, aspiration performed to prove the point of the needle not to be in a blood vessel, and 30 ml. of 1% procaine hydrochloride solution containing 20 drops of 1 in 1000 adrenaline per 100 ml. injected. The viscera fall back into the abdomen and render it easy to inject a further 10 ml. of the solution to the left of the aorta behind the oesophagus.

The most commonly used local anaesthetic in abdominal surgery is procaine hydrochloride, 1% solution, with adrenaline, 1 in 1000. A new local anaesthetic, procaine hydrochloride in 1% solution can be used without injury. In cardiac and arterial patients, 1% cocaine (up to 500 ml.) is used instead of adrenaline. In patients with arterial disease, add 1 in 1000 adrenaline to the 1% cocaine solution. In patients with arterial disease, add 1 in 1000 adrenaline to the 1% cocaine solution.

**Choice of Methods of Anaesthesia—**

**ANTERIOR SPLANCHNIC** for radical operation after exploratory laparotomy.  
**PARAVERTEBRAL**, in resections of large intestine to mobilise the fixed colon: for the resection.

*Mesenteric anaesthesia* added.

**PARASACRAL** sufficient for operations on rectum and perineum.

**EPIDURAL (SACRAL)** sufficient for pelvic operations.

**SPINAL anaesthesia** now little used in Germany owing to danger of fall of blood pressure and danger to respiratory centre.

*Combined parasacral* safer and efficient for longer time.

Prof H. Finsterer, *Brit. med. J.*, 11/1932, 400.

[P1] **Injectio Procainæ et Adrenalinæ (R L O H)**. *Syn.* INJECTIO NOVOCAINÆ ET ADRENALINI.

Procaine hydrochloride 8 or 16 gr., solution of adrenaline hydrochloride 24 m., sterilised water to 1 oz. (approx. 2 or 4%). *Dose.*—Up to 1 drachm of the 2%. In eye work may be employed, e.g., for excision of the lachrymal sac, and for other minor operations

[P1] **Solutio Novocainæ Composita (St T H)**. *Syn.* DUNHILL'S SOLUTION.

Novocain 3 gr., solution of adrenaline hydrochloride 7½ m., sodium chloride 14 gr., water to 3½ oz

[P1] **Arecan (Evans, Sons, Lescher & Webb, Liverpool)** Solutions of procaine hydrochloride with adrenaline in various strengths

[P1-81] **Duracaine (Pharmaceutical Specialities (May & Baker) Ltd., London)**. Solution of Planocaine in 15% alcohol with gum acacia for intraspinal anaesthesia. Issued as (1) light solution—s.g. 1.002, ampoules of 3 ml., (2) heavy solution—s.g. 1.028, ampoules of 3.5 ml.

[P1] **Neotonocain (Richter, London)**. Novocain and adrenaline in various strengths.

[P1] **Novophedrin (Richter, London)** 2 ml. ampoules containing procaine hydrochloride 0.04 g. and ephedrine hydrochloride 0.05 g. Local anaesthetic for dental use. A 4% solution (0.08 g. procaine hydrochloride) is issued as a local anaesthetic.

[P1] **Novutox (Pharmaceutical Corporation, London)**. Procaine with isooctyl-hydrocupreine hydrochloride. A self-sterilising solution of procaine.

[P1] **Parasetic (Parke, Davis, London)**. Procaine hydrochloride 2.25%, adrenaline chloride 1/30,000.

[P1-81] **Spinocain (Bayer Products, London)** Each 2 ml. ampoule contains 0.2 g. of Novocain, 2.2 mg. of strychnine sulphate, and 14½% of alcohol in normal saline. It also contains gliadin or amyloprolamin.

The amount stated is mixed with more or less cerebrospinal fluid as required, and after injection the table is tilted to direct it to any region desired. In the circumstances of a modern operation a large fall of blood pressure is not greatly to be feared. Jonnesco gave up strychnine after 15 years' trial. A similar solution to Spinocain, but without the strychnine, gave equally good results. No evidence to show that addition of dextrin is not as good as gliadin.—E. Falkner Hill, *Lancet*, 1/1930, 124

Thought to be an improvement on Stovaine, the use of which was often followed by collapse.—C. L. Granville Chapman, *Brit. med. J.*, 1/1930, 799; see also R. A. Grant, *Brit. med. J.*, 1/1930, 1090

Spinal anaesthesia with Spinocain, using Ephedrine-Novocain first. 250 cases.—A. Wilfred Adams, *Brit. med. J.*, 1/1931, 785. Death under.—A. Wilfred Adams, *ibid.*, 1/1931, 869.

[P1-81] **Borocaine (Sharp & Dohme, Philadelphia; British Drug Houses, London)**. PROCAINE BORATE.

$2(C_{13}H_{20}O_2N_2) \cdot 5B_2O_3 \cdot 4H_2O$ . Available as the substance and in tablets with or without adrenaline. Although a salt of procaine, it is stated to be more active but less toxic than procaine hydrochloride. The difference in properties is due to the fact that Borocaine, being the salt of a weak acid, in solution yields free alkaloidal base by hydrolysis.

For ophthalmic and dental use, for operations on and examination of the urethra and bladder, and for surface anæsthesia in general, 2% solutions are used, and for operations on the nose and throat 5% solutions. (Beta-Borocaine, *v. antea*, is stated to be a better surface anæsthetic.)

An account of the borates of some anæsthetic bases ("borocaines") —A J Copeland and H E F. Notton, *Brit med J*, 11/1925, 547

A 2% solution of Borocaine is an improvement on a 0.5% solution of cocaine, in urethral anæsthesia, and a 1% solution of the former gives better anæsthesia than a 0.5% solution of cocaine, but a 0.5% solution of Borocaine has no advantage over a 0.3% solution of cocaine. Beta-eucaine borate in 0.5% solution is a perfect urethral anæsthetic and the relaxation is perfect. In  $\frac{1}{2}$ % its action is equal to  $\frac{1}{4}$ % cocaine hydrochloride, but  $\frac{1}{2}$ % is not so good as  $\frac{1}{4}$ % cocaine — R Coyte, *Brit med. J.*, 1/1926, 85

OPHTHALMOLOGY. Borocaine greatly inferior to cocaine as regards surface anæsthetic effect. Cocaine is perfectly reliable, whereas the effect of Borocaine is variable —T H Butler and R U Gillan, *Brit med J*, 1/1926, 84

### Other Proprietary Local Anæsthetics.

[P1 81] **Acoine** (Heyden, Dresden, Braun, London) Di-*p*-anisyl-monophenetylguanidine hydrochloride. A local anæsthetic soluble in water. For infiltration anæsthesia in 0.5 to 1% solution, and specially suitable as anæsthetic for mucous membranes

[P1 81] **Butesin Picrate** (Abbott, Montreal; Pharmaceutical Products, London). The picric acid salt of Butesin, which is the butyl ester of 4-aminobenzoic acid. Supplied in the form of [P1] 1% ointment or [P1] 5% dusting powder. An analgesic-antiseptic for burns, scalds, ulcers, abrasions, etc.

Four cases of eruption following the use of Butesin picrate ointment —M B Sulzberger and F Wise, *Arch Derm Syph*, 1933, 461.

[P1 81] **Butyn** (Abbott, Montreal, Pharmaceutical Products, London). *p*-Aminobenzoyl- $\gamma$ -di-*n*-butylaminopropanol sulphate. Dose.—By hypodermic injection 1 ml and upwards of  $\frac{1}{2}$  or more per cent. solution according to circumstances. A white amorphous powder, freely soluble in water. Incompatible with chlorides and salicylates.

A local anæsthetic quicker and more profound in action than cocaine. When used in eye work, accommodation is not paralysed. For removing foreign bodies from the eye a drop of 1% solution almost immediately produces anæsthesia.

The absence of dilatation of the pupil justifies its use in glaucoma as an analgesic in combination with eserine or pilocarpine. Operations on the muscles by infiltration with 0.5% solution —W M Beaumont, *Lancet*, 11/1922, 304.

In operative eye work 1 to 2% Butyn solution used. For profound anæsthesia 4 or 5%. Four applications at intervals of 2 minutes. 2%, applied topically, also suited for nose, ear and throat, e.g., septum resection, tonsillectomy and adenoids. In dental work 10 drops or more of  $\frac{1}{2}$ % solution, on opposite sides of the tooth to be extracted, with or without adrenaline, allow one minute to elapse. For genito-urinary work 2% used —W. M. Beaumont, *Brit med J*, 1/1923, 57

Butyn is quite as toxic as cocaine and less efficient —*Lancet*, 11/1923, 1297. Possibly "habit forming." —A J. Copeland, *Brit. med J*, 11/1924, 41

Contraindicated where there is a solution of continuity in the mucous membrane, either through trauma or ulceration, as this allows too rapid absorption of the drug. —W. R. Jamieson, *J. Amer. med. Ass.*, 1/1929, 1519.

[P1 81] **Butyn Oral Obtundent** (*Abbott, Montreal, Pharmaceutical Products, London*) Butyn sulphate 10%, alcohol (95%) 10%, aqueous solvent 80% For topical application as a local anæsthetic in dental work

[P1] **Butyn Sterules** (*Martindale, London*) contain 1 ml of 1% or 2% solution

[P1 81] **Decicain** (*Bayer Products, London*) (Formerly known as Pantocain) *p*-Butylaminobenzoyldimethylaminoethanol hydrochloride, a local anæsthetic of the procaine series. In white crystals, m.p. about 150°, soluble in water and alcohol. For surface anæsthesia, 1 to 2% solution, for infiltration anæsthesia, 1 in 1000 solution in normal saline with adrenaline. For spinal anæsthesia, 1.5 to 2 ml. of ½% solution. Available in powder, tablets of 0.1 g., 2% solution, and ½% solution in ampoules.

[P1 81] **Decicain L** is a viscous solution of Decicain for spinal anæsthesia issued in ampoules containing 0.03 g. in 3.75 ml., also in 2 ml. ampoules containing 0.002 g. of Decicain and 0.1 g. of Racedrin (racemic ephedrine).

**Diocaine** (*Ciba, London*) *p*-Diallyloxyethyl-diphenyldiamidine hydrochloride. A local anæsthetic for ophthalmic purposes. Supplied in powder for making a 0.2 or 0.5% solution.

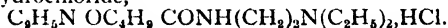
**Impletol** (*Bayer Products, London*) A molecular compound of diethyl-*p*-aminobenzoyl hydrochloride and caffeine.

*Dose* — 2 ml. subcutaneously or intramuscularly. In migraine, dysmenorrhœa and pain due to vasomotor disturbances.

[P1 81] **Metycaine** (*Lilly, London*) Hydrochloride of  $\gamma$ -(2-methyl piperidino)-propyl benzoate. A local anæsthetic employed as 2% solution.

[P1 81] **Panthesine** (*Sandoz, London, Brooks & Warburton, London*) N-Diethyl-leucinol ester of *p*-aminobenzoic acid. A local anæsthetic stated to have a surface anæsthetic action equal to that of cocaine with only one-third the toxicity. Issued in solution and ampoules and as powder. [P1] **Panthesine Balm** containing 5% of Panthesine is indicated in rheumatism, gout, neuralgia, etc.

[P1 81] **Percaine** (*Ciba, London*). (*Syn* NUPERCAINE in U.S.A.). The hydrochloride of  $\alpha$ -butyloxycinchonic acid diethylethylenediamide or 2-butyloxyquinolinecarboxylic acid-4-diethylethylenediamide hydrochloride,



It is supplied as base or hydrochloride and in 2% solution (for surface anæsthesia), also in solutions of various strengths for spinal anæsthesia, and in solution and tablets with adrenaline.

*Dose* — For infiltration anæsthesia solutions of from 1 in 2000 to 1 in 10,000 with addition of 0.1 ml. of adrenaline hydrochloride solution (1 in 1000) to 100 ml. Not more than 100 ml. of 1 in 1000 solution should be injected. For spinal anæsthesia from 7.5 to 10 mg. in 1 in 200 solution. For sacral anæsthesia 25 to 35 ml. of 1 in 1000 solution. Solutions should be prepared with distilled water, and alkali-free glass used.

Colourless crystals, m.p. 97°. Readily soluble in water and alcohol. Solutions are made in normal saline, giving neutral solutions.

**Toxic Effects.** Fatal syncope following Percaine in operation for a large ovarian cyst occupying the abdomen up to the costal margin. The prone position is an error. It should be remembered that the gravid uterus is a similar contraindication.—W. Howard Jones, *Lancet*, ii/1930, 550.

Used as a local anæsthetic in abdominal surgery, caused necrosis of the tissues. Prof. Finsterer (Vienna) reported two deaths within 24 hours following its use.—*Brit. med. J.*, ii/1932, 400.

Two deaths following lumbar anæsthesia with 2 ml. and 10 ml. of 0.4% solution. Severe lesions in spinal cord, membranes, and nerve roots.—*Per Brit. med. J. Epit.*, ii/1933, 95.

**Uses.** A local anæsthetic, acting like cocaine when applied to mucous surfaces and like cocaine or procaine when injected, the action being relatively prolonged. It is about five times as toxic as cocaine when injected intravenously into animals, and is many times more active than procaine hydrochloride when injected subcutaneously.

*For details of use of Percaine in oil in the treatment of pruritus ani and anal fissure, see p. 395.*

It is potent in such high dilution that the content adds next to nothing to the sp. gr. of the vehicle. For thoracic nerve root blocks, solutions 1 in 2000 to 1 in 1000 according to duration of analgesia needed. 7½ to 10 mg. said to be more effective than 150 mg. of procaine hydrochloride.—W. Howard Jones, *Lancet*, i/1930, 573.

Mucous membranes, especially of the nose, anæsthetised with 1 and 2% solutions, with addition to each 50 ml. of ¼ ml. of adrenaline solution, for partial resections of turbinates, removal of polypi, ethmoidal curettages, and intranasal drainage of maxillary antrum. The mucous membrane is not permeated, though profoundly affected.—O. Popper, *Brit. med. J.*, i/1930, 669.

Has far greater toxicity and no great advantage over Novocain-adrenaline for infiltration anæsthesia but promising for mucous membranes.—M. C. G. Israels and A. D. Macdonald, *Brit. med. J.*, ii/1931, 986.

The least toxic of the spinal analgesics. Effect on blood pressure considerably less; the effect lasts from 1 to 3 hours and the patient is free from pain for from 6 to 12 hours after the operation, while a smaller number of headaches occur than with Stovaine, etc. High abdominal anæsthesia can be produced with maximum of safety, and the same solution used to infiltrate the skin before introducing the intrathecal needle. The dilute solution (20 ml. of a 1 in 1500 solution) is more often used, but the stronger (2.3 ml. of a 1 in 200) is useful for operations on the perineum, etc., using doses of 0.6 ml. up to 2.3 ml., and operations such as removal of piles, cystoscopy and prostatectomy may be done with this strong solution. Premedication with Omnopon and scopolamine is given one hour before operation. Howard Jones' technique described, as used in 1200 cases. Injection in the upright sitting position the technique of choice for pregnancy, patients with large abdominal tumours, and similar cases.—R. Jarman, *Brit. med. J.*, i/1934, 797.

Prof. Sebrechts, of Bruges, from an experience of 35,000 cases, considers spinal anæsthesia with Percaine the method of choice for abdominal surgery, using 15 to 20 ml. of the 1 in 1500 solution in fractional doses of 5 ml. at 5-minute intervals. Individuals vary in their reaction, ignorance of which probably accounts for most of the former failures and disasters. An injection of ½ gr. of morphine and ½ gr. of scopolamine an hour before operation helps in estimation of patient's response, the sensitive being deeply narcotised; the normal, somnolent; and the resistant unaffected.—*Brit. J. Anæsth.*, Oct., 1934, 4.

[P1 81] **Unguentum Sedativus (St. T.H.).** Percaine (base) 2, liquefied phenol 1.25, solution of hamamelis 10, simple ointment 86.75.

[P1 81] **Percainol (Ciba, London).** Ointment containing 1% of Percaine with solution of hamamelis and aluminium formate. Anti-pruritic and analgesic application for skin diseases.

[P1 81] **Phenolaine (Phenolaine Co., London).** The preparation is stated to contain methyl, ethyl, benzoic and carboxyl groups and

an amine group. It has been used in a large number of operations without trouble as regards bleeding or subsequent after-effects. It does not produce vasodilatation on subcutaneous or intramuscular injection.

**Dose.**—For general surgery, *e.g.*, for hernia or appendicitis, use 2 drops of Phenolaine to each ounce of sterile water. Not more than 6 ounces of the dilution should be used at one time. For teeth extraction use 8 drops to 1 ounce of water. Amputations of the breast have been conducted with 12 drops in 6 ounces of water.

[P1] **Scuroforme** (*Pharmaceutical Specialties (May & Baker) Ltd., London*). Butyl-*p*-aminobenzoate. Local anæsthetic where prolonged and rapid anæsthesia is required. Applied as powder, solution in oil or in alcohol and glycerin.

[P1 S1] **Tutocaine** (*Bayer Products, London*) *p*-Aminobenzoyldimethylaminomethylbutanol hydrochloride.

Used as local anæsthetic in 0.2 to 1% solution

Tutocaine has about one-third the toxicity of cocaine, and is rather more than twice as toxic as procaine hydrochloride. From clinical observations a 5% Tutocaine solution has the same anæsthetic effect as a 3½% cocaine solution —E. Watson-Williams, *Lancet*, 1/1925, 913.

For both infiltration and surface anæsthesia the minimal effective concentration of Tutocaine is ½ that of cocaine or Psicaine (about 0.013% for cocaine). The minimum lethal doses for guinea-pigs were: Cocaine 0.05, Psicaine 0.1 and Tutocaine 0.2 g. per kilo. The efficiencies, calculated as the ratio of lethal dose to minimum effective dose, were 4, 6.3 and 64.5 respectively. The anæsthesia is lengthened by the addition of adrenaline to the solutions. The addition of phenol in small amounts increases potency in surface anæsthesia —W. Wagner, *Arch. exp. Path., Pharmacol.*, 1925, 109, 64.

The most suitable strength for urethral work is ½ to ¼% with adrenaline. —*Per Prescriber*, Jan., 1927, 7.

Tutocaine more toxic than procaine hydrochloride, but quicker in action. 1 in 500 solution proved a reliable anæsthetic —H. V. Molesworth, *Brit. med. J.*, 1/1930, 13

## CODEINA

*B.P.*, *U.S.P.* XI, *P. Ned.* V, *P. Ital.* V, *Fr. Cx.*, *P. Helv.* V, *P. Dan.*, *F.E.* VIII, *P. Belg.* IV.



[P1] "Alkaloids, the following; their salts, simple or complex:—*Codeine*."

[S1] "Alkaloids, the following; their salts, simple or complex:—*Codeine* except substances containing less than 1% of codeine."

**Note.**—Although codeine and its salts are controlled by the *Methylmorphine and Ethylmorphine Regulations, 1933*, these regulations do not affect any sale or distribution by an authorised seller of poisons in the course of any retail business (see page 1034).

Codeine is not really dangerous as an addiction drug.—Sir W. Willcox, *Pharm. J.*, 15/1924, 28.

*Codeine and Dangerous Drugs Act, 1932.*—It was argued at the 1925 Geneva Convention that codeine could be converted into drugs of addiction. Codeine



being usually manufactured from morphine, it is open to a manufacturer, if codeine remains exempt from control, to buy codeine in the open market without the knowledge of the Government, he can then divert a corresponding amount of morphine into the illicit traffic and explain its disappearance by saying that he has converted it into the codeine. It was finally agreed that the restrictions should only relate to manufacture, export and wholesale trade—*Brit med J Supplement*, Mar 5, 1932.

Codeine has a relatively feeble euphoric action, and the addict can get little satisfaction from the drug taken by the mouth, but large doses of codeine taken hypodermically or intravenously can act as a morphine substitute for the addict. Doses as large as 80 grains hypodermically every day have been reported—*Canad med Ass J*, 1935, 424.

**Dose.**— $\frac{1}{4}$  to 1 grain (0.016 to 0.06 g.) *Fr Cv.* has maximum single dose  $\frac{3}{4}$  grain, maximum during 24 hours 3 grains approximately. *P Dan.*, *P Ital* and *P Belg.* are similar. *P Helv V* has  $1\frac{1}{2}$  and 5 grains respectively. *U S P. XI* average dose  $\frac{1}{2}$  grain.

An alkaloid from opium or from morphine, in nearly colourless trimetric crystals, melting, after drying at  $100^{\circ}$ , at  $155^{\circ}$  to  $156^{\circ}$ . It is a methyl ether of morphine—monomethyl-morphine.

**Soluble** 1 in 120 of water, 1 in 2 of alcohol 90%, 1 in 13 of benzene, 1 in 20 of ether, also in chloroform and in excess of aqueous ammonia, but insoluble in excess of potash solution, very soluble in dilute acids.

**Antidotes.** Treat as for poisoning by morphine, *see p. 638*.

**Uses.** In moderate doses is hypnotic and in frequent small doses it allays cough in phthisis. For cough following catarrh  $\frac{1}{4}$  to 1 grain gives relief. In diabetes, beginning with  $\frac{1}{4}$  grain thrice daily it lessens the amount of sugar in the urine. A useful sedative in chronic cystitis with enlarged prostate.

**[P1 81] Capsulæ Codeinæ et Valerianæ Compositæ.**

**Dose**—1 or more *p d* according to strength.

Codeine  $\frac{1}{4}$  to 1 gr., extract of valerian 2 gr., phenol 2 gr., extract of cascara  $1\frac{1}{2}$  gr. In glycosuria, codeine is valuable for treatment, the valerian is a nerve sedative and the phenol is an intestinal disinfectant.

**[P1 81] Capsulæ Codeinæ cum Extracto Cannabis.**

Codeine  $\frac{1}{4}$  gr., extract of cannabis  $\frac{1}{4}$  gr.

In neuralgia, 1 every 4 or 5 hours.

**[P1] Gelatinum Codeinæ (B P C). Syn. CODEINE AND GLYCERIN JELLY.**

**Dose**—1 drachm (4 g.) A lemon-flavoured preparation containing about 0.2% of codeine, equivalent to about  $\frac{1}{4}$  gr. in 1 drachm.

Useful in chronic laryngitis, phthisical cough, etc. Also in ulcer of the stomach.

**[P1] Pastilli Codeinæ (B P C)** contain  $\frac{1}{4}$  gr. (0.008 g.)

**[P1 81] Pilula Codeinæ Composita.**

Codeine  $\frac{1}{4}$  gr. (increased to 2 gr. if necessary), extract of nux vomica  $\frac{1}{4}$  gr., extract of lettuce  $\frac{1}{4}$  gr. or more, mucilage *q s* to make one pill. To be taken 2 or 3 times a day, for diabetes.

**[P1 81] Codeinæ Hydrobromidum.**

$C_{18}H_{21}O_3N.HBr.2H_2O = 416.1$

An anti-spasmodic similar in dose and use to the phosphate. For eye work has been advised to take the place of ethylmorphine—being said to cause less pain.

**[P1 81] Codeinæ Hydrochloridum** (*P. Ned V*, *P. Ital. V*, *P. Helv. V*, *P. Dan.*).  $C_{18}H_{21}O_3N.HCl.2H_2O = 371.7$ .

**Dose.**— $\frac{1}{4}$  to 2 grains (0.016 to 0.12 g.). White crystalline powder, soluble 1 in 30 of water.

[P1 81] **Codeinæ Periodidum.**  $C_{17}H_{18}(CH_3)O_3N \cdot 2I = 553.0$

*Dose.*— $\frac{1}{4}$  to  $\frac{1}{2}$  grain (0.016 to 0.03 g.)

A yellowish-brown powder containing about 54% of codeine. Combines the action of codeine with the antiseptic action of iodine.

[P1 81] **Codeinæ Phosphas** (*B.P.*, *U.S.P. XI*, *P. Jap.*, *Fr. Cx.*, *P.G. VI*, *P. Helv. V*, *P. Dan.*, *P. Ital V*, *P. Belg IV*).

$C_{18}H_{21}O_3N \cdot H_3PO_4 \cdot H_2O = 415.2$  *U.S.P. XI* has  $1\frac{1}{2} H_2O$ .

*Dose.*— $\frac{1}{4}$  to 1 grain (0.016 to 0.06 g.) *Fr Cx* has max during 24 hours 5 grains approximately

In granular snow-white crystals, containing 69% of anhydrous alkaloid. Is suitable for hypodermic injection, 1 grain in 15 minims (1 ml.)

**Soluble** 1 in 3.5 of water, 1 in 350 of alcohol 90%, sparingly soluble in ether and chloroform

[P1] **Linctus Codeinæ** (*B.P.C.*)

*Dose* —  $\frac{1}{2}$  to 1 drachm (2 to 4 ml.)

Contains codeine phosphate  $\frac{1}{2}$  gr with citric acid, emulsion of chloroform, glycerin and mucilage of tragacanth to 1 drachm

[P1 81] *St T H* has syrup of codeine phosphate 50% *v/v* in similar vehicle

[P1] **Linct. Codein. Co.** (*N.I.F.*)

Syrup of codeine phosphate and syrup of virginian prune, equal parts

[P1 81] **Pilulæ Codeinæ et Belladonnæ** (*C.X.H.*)

Codeine phosphate  $\frac{1}{2}$  gr, dry extract of belladonna  $\frac{1}{2}$  gr, kaolin  $2\frac{1}{2}$  gr, hard soap to 4 gr

A combination of two drugs with marked antispasmodic action and power to relieve pain originating in plain muscle. Designed for administration in painful colic spasm. To be taken regularly over a period of weeks for full effect —E. C. Warner, *Practitioner*, 1935, 831

[P1] **Syrupus Codeinæ Phosphatis** (*B.P.C.*)

*Dose* —  $\frac{1}{2}$  to 2 drachms (2 to 8 ml.)

Codeine phosphate 0.5% in a solvent of distilled water and syrup. Contains about  $\frac{1}{4}$  gr of codeine phosphate per drachm.

[P1 81] **Codeinæ Sulphas** (*U.S.P. XI*).

$(C_{18}H_{21}O_3N)_2 \cdot H_2SO_4 \cdot 5H_2O = 786.5$

*Dose* —  $\frac{1}{4}$  to 1 grain (0.016 to 0.06 g.)

White crystals efflorescent in air; soluble 1 in 40 of water, slightly soluble in alcohol

Given with advantage in sciatica, also in morphine habit, *q.v.*

[P1 81] **Codeine Methylbromide.**

$C_{17}H_{18}CH_3O_3N \cdot CH_3Br = 394.2$  *Syn. EUCODEINE.*

*Dose.*— $\frac{1}{4}$  grain (0.05 g.) Is less toxic than codeine.

**Apocodeinæ Hydrochloridum.**  $C_{18}H_{19}O_3N \cdot HCl = 317.6$ .

*Dose* —  $\frac{1}{10}$  gr. gradually increased to 1 grain (0.006 to 0.06 g.) 3 or 4 grains daily may safely be given. A greyish, hygroscopic powder consisting of the salt of the base or mixture of bases obtained by the action of zinc chloride on codeine.

**Soluble** in water, less soluble in alcohol.

**Uses.** Is a sialagogue and sedative, and increases peristalsis

Is more expectorant than apomorphine and less emetic. Hypodermically 30 minims of 1% solution ( $= \frac{1}{3}$  gr.) may purge in half an hour or less, but may also prove emetic.

[P1] **Codoforme Botal Tablets** (*Bottu, Paris; Continental Laboratories, London*). A laryngeal sedative for all forms of cough. *Dose*.—1 to 5 tablets daily according to age and the nature of the cough. Each tablet is stated to be equivalent to codeine  $\frac{1}{4}$  gr., bromoform 4 m., tincture of aconite 1 m., tincture of belladonna 1 m., with terpine  $\frac{1}{8}$  gr. and sodium benzoate  $\frac{1}{2}$  gr.

[D-P1-81] **Dicodid** (*Knoll, Ludwigshafen; Pharmaceutical Products, London*). Dihydrocodeinone acid tartrate (for oral use) or hydrochloride (for subcutaneous injection). In white crystals soluble in water. Its activity is midway between that of morphine and codeine with specific influence on the cough centre. Tablets contain  $\frac{1}{8}$  gr. or  $\frac{1}{4}$  gr. Ampoules contain  $\frac{1}{2}$  gr.

*Dose*.—For cough and less severe pain  $\frac{1}{8}$  gr. orally, 2 or 3 times daily, increased if necessary. Subcutaneously, half to one ampoule. Should not be administered on an empty stomach

[D-P1-81] **Dilaudid** (*Knoll, Ludwigshafen; Pharmaceutical Products, London*). *Syn.* DIHYDROMORPHINONE HYDROCHLORIDE.  $C_{17}H_{19}O_3N.HCl = 321.6$ .

*Dose*.— $\frac{1}{8}$  gr. per os or  $\frac{1}{4}$  gr. subcutaneously. This dose is effective for 4 to 6 weeks without increasing.

Has a chemical structure analogous to that of Dicodid. Soluble in water and alcohol, insoluble in ether. The analgesic effect of  $\frac{1}{4}$  gr. of Dilaudid is equivalent to that of  $\frac{1}{2}$  gr. of morphine. It is not suitable for infants.

Tablets are available containing 0.0025 g. of the hydrochloride. Also issued in ampoules containing 0.002 g. in 1 ml., and in combination with scopolamine hydrochloride 0.0003 g., and with atropine sulphate 0.0003 g.

Introduced to reduce the undesirable secondary effects of morphine. In post-operative pain effective in dose of  $\frac{1}{2}$  the corresponding dose of morphine. Tends to prevent sleep. No vomiting or headache.—*Per Quart. J. Pharm.*, 1929, 358

Used with beneficial effects in pleurisy, sciatica, facial neuralgia, angina pectoris, and acute arthritis, to replace morphine, but of no value when morphine addiction has developed. Unlike morphine, it is not necessary to increase the dose. It may cause transient nausea, giddiness, and confusion, but does not cause constipation or affect the appetite.—O. Leyton, *Lancet*, 1/1932, 835

The tranquillising potency of Dilaudid as judged by its depressant action on the spontaneous discomfort movements of rats, is ten times that of morphine. The respiratory depressant action is also ten times that of morphine. In doses producing equal sedative effects, Dilaudid does not differ significantly from morphine in its respiratory depressant action. Dilaudid possesses definite addiction liability in rats, essentially identical with that of morphine in doses of equal tranquillising potency. Tolerance develops to the daily administration of Dilaudid to the same degree as to that of morphine. The toxicity of Dilaudid upon daily administration, as judged by weight changes, is almost ten times that of morphine.—E. J. Stanton, *J. Pharmacol.*, 1936, 56, 262.

[D-P1-81] **Sterules of Dilaudid** (*Martindale, London*) contain 0.002, 0.004 and 0.005 g. in 1 ml.

[D-P1-81] **Eukodal** (*Merck, Darmstadt; Martindale, London*).

DIHYDROXYCODEINONE HYDROCHLORIDE,  $C_{18}H_{21}NO_4.HCl = 351.6$ .

**Dose.**— $\frac{1}{4}$  gr. (0.005 g.) *per os*, or  $\frac{1}{4}$  to  $\frac{1}{2}$  gr. (0.01 to 0.02 g.) subcutaneously.

White crystalline powder soluble in water. M.p. 270°.

Analgesic and hypnotic, used as a substitute for morphine; it is less toxic and shows less by-effects.

**Eukodal, Dico did and Dilaudid.** Eukodal differs from Dilaudid and Dico did in that it does not cause convulsions, and very large doses are needed to cause death. The toxicity of Dilaudid is much greater than Dico did. The pharmacological actions of all of them are very similar to morphine, but they are much more toxic, smaller amounts of Dilaudid than morphine are needed to depress the respiratory centre. Eukodal has a much weaker action on the movements of the alimentary tract than the other two, and does not increase special reflexes, but it has a profound effect on respiration, as marked as that produced by either Dilaudid or morphine. There is no reason to think that any of these drugs are superior to morphine from a therapeutic point of view.

—G. N. Myers, *Brit med J*, 1/1933, 981

Pharmacological action of Dilaudid, Dico did and Eukodal —G. N. Myers, *Brit. med. J*, 11/1933, 282

**Paracodin** (Knoll, Ludwigshafen; *Pharmaceutical Products, London*). Dihydrocodeine. Tablets contain  $\frac{1}{2}$  grain. **Dose.**—1 to 3 tablets thrice daily. Indications as for codeine. **Paracodin Syrup** contains 0.2% of Paracodin

## COLCHICUM

[P1] "*Alkaloids, the following; their salts, simple or complex:—Colchicine.*"

[S1] "*Alkaloids, the following; their salts, simple or complex:—Colchicine except substances containing less than 0.5% of colchicine.*"

[P1] **Colchici Cormus** (B.P.).

**Dose.**—2 to 5 grains (0.12 to 0.2 g.) of the dried corm.

The corm of the meadow saffron, *Colchicum autumnale* (Liliaceæ). Both fresh and dried corm are official, although the former is not used in making any preparations. The dried corm contains not less than 0.25% of colchicine.

**Toxic Action.** Colchicum affects the gastro-intestinal membrane. It may cause pains in the bowels, vomiting, diarrhœa, intense thirst, and violent burning in the throat, œsophagus and stomach.

**Antidotes.** Empty stomach by emetic, or by stomach tube using dilute tannic acid solution. Give repeated large doses of medicinal charcoal. Keep patient warm; give demulcent drinks freely. Dextrose may be administered intravenously, or saline infusion may be necessary. Atropine,  $\frac{1}{100}$  gr., and morphine,  $\frac{1}{4}$  gr., hypodermically to check diarrhœa. Strychnine,  $\frac{1}{4}$  gr., or caffeine sodium benzoate, 2 gr., hypodermically for collapse.

**Uses.** Has specific effect in gout, relieving pain and reducing inflammation in the acute attack, but has no prophylactic action. It may be given in pill with ipecacuanha and mercury, or as the tincture in mixtures. To abolish the vomiting and diarrhœa often produced, a small dose of atropine may be given with it.

**[P1-81] Extractum Colchici Aceticum (B.P.C.)**

*Dose.*— $\frac{1}{4}$  to 2 grains (0.03 to 0.12 g.).

An unstandardised soft extract prepared by evaporating the juice of the corm to which acetic acid has been added

**[P1 81] Extractum Colchici Siccum (B.P.)**

*Dose.*— $\frac{1}{4}$  to 1 grain (0.016 to 0.06 g.).

The 60% alcohol extractive adjusted with lactose to contain 1% of colchicine. *Fr. Cx.* extracts seeds with 70% alcohol, not standardised. Max. single dose  $\frac{3}{4}$  grain, max. in 24 hours 3 grains approx. *P Ital V* extracts with alcohol 60% standardising to 2% of colchicine, *P. Belg. IV* and *F.E VIII* use 70% with same standard.

**[P1] Liquor Antirheumaticus Compositus.**

*Dose.*—30 minims (2 ml.)

Colchicum wine 15, spirit of ether 5, camphor 2, compound tincture of lavender to 30.

**[P1] Pilulæ Colchici et Aloes (B.P.C.).**

*Dose.*—1 to 4 pills

Contain  $\frac{1}{4}$  gr. each of dry extract of colchicum, dry extract of hyoscyamus and aloes

**[P1] Pilulæ Colchici et Hydrargyri (B.P.C.)**

*Dose.*—1 to 3 pills

Contain  $\frac{1}{8}$  gr. of dry extract of colchicum,  $\frac{1}{4}$  gr. of pill of mercury and  $\frac{1}{4}$  gr. of compound extract of colocynth

**[P1] Pilulæ Colchici et Hydrargyri Compositæ (B.P.C.) *Syn* BRODIE'S GOUT PILLS**

*Dose.*—1 or 2 pills

Contain  $\frac{1}{4}$  gr. of dry extract of colchicum and 14 gr. each of pill of mercury, compound extract of colocynth and extract of rhubarb.

**[P1] Vinum Colchici (B.P.C.)**

*Dose.*—10 to 30 minims (0.6 to 2 ml.)

1 of corm in 5 of sherry-type wine

Is given in mixtures with alkali and magnesium sulphate

In gout, controls the inflammation 30 minims as first dose, then 15 minims every 3 hours. It is not objectionable to the taste

**Pistoia Gout Powder.** *Syn* POLVERE ANTIGOTTOSO (*Farmacia Benedettine, Pistoia*) Stated to contain *Gentiana lutea* 30, *Smilax china* (China root) 30, *Jateorhiza palmata* 20, *Aristolochia rotunda* (birthwort root) 10, *Artemisia Abrotanum* (Southernwood) 10

**[P1] Colchici Semen (B.P.).**

*Dose.*—2 to 5 grains (0.12 to 0.3 g.)

Contains not less than 0.3% of colchicine. *U.S.P XI* requires not less than 0.45%, *P. Ital. V* and *P. Belg IV* 0.4%, *F.E VIII* 0.45%; *P. Helv. V* 0.5%. *I.A.* requires all preparations to be made from the seed.

**[P1] Extractum Colchici Liquidum (B.P.) *Syn.* Fluid-extractum colchici.**

*Dose.*—2 to 5 minims (0.12 to 0.3 ml.)

Contains 0.3% w/v of colchicine.

**[P1] Mist. Colchici c. Sod. Sal. (N.I.F.).**

Sodium salicylate 10 gr, solution of burnt sugar 5 m, potassium bicarbonate 15 gr, liquid extract of colchicum 3 m, peppermint water to  $\frac{1}{2}$  oz.

**[P1] Tinctura Colchici (B.P.)**

Dose —5 to 15 minims (0.3 to 1 ml). *Fr. Cx* (1 in 10) has max single dose 25 minims, max daily dose 100 minims.

Contains 10% *v/v* of liquid extract, equivalent to 0.03% *w/v* of colchicine.

**[P1] Tinctura Colchici Seminls (U.S.P. XI)      Syn TINCTURA COLCHICI, U.S.P. X**

Average dose —30 minims (2 ml)

Colchicum seed, 1 in 10 Is one third stronger than Tinctura Colchici B.P.

**[P1] Vinum Colchici Seminls (B.P.C.)**

Dose —10 to 30 minims (0.6 to 2 ml)

Colchicum seed, 1 in 10, in detannated sherry-type wine.

**[P1] Colchici Flos.** The fresh perianth of the meadow saffron It has similar properties to the corn

**[P1 81] Colchicina (B.P.C., *Fr. Cx*, F.E. VIII, P. Dan., U.S.P. XI).**  $C_{22}H_{25}O_6N = 399.2$  *P. Helv. V* has  $\frac{1}{2}H_2O$ . *P. G. VI* has  $C_{22}H_{25}O_6N, \frac{1}{2}CHCl_3$  which contains 87% of colchicine

Dose — $\frac{1}{16}$  to  $\frac{3}{16}$  grain (0.0005 to 0.002 g) in a pill *P. Dan.* and *Fr. Cx.* have maximum single dose  $\frac{1}{8}$  grain, max. during 24 hours  $\frac{1}{8}$  grain approximately *U.S.P. XI* average dose  $\frac{1}{16}$  grain

*Intravenously* has been tried in dose of  $\frac{1}{160}$  grain with sodium iodide and sodium salicylate 1 g each in 20 ml.

Yellowish flakes, crystals or powder, with a hay-like odour when dampened and warmed It is a weak base, most of its salts being decomposed by water

**Soluble** 1 in 22 of water with neutral solution, readily in alcohol 90% but less in dehydrated alcohol, very soluble in chloroform, slightly soluble in ether (1 in 155).

Of use in acute gout, rheumatic gout, asthma, cerebral congestion and uræmia

**[P1 81] Pilula Colchicinae, Hyoscyami et Nucis Vomicae.**

Dose —1 every 3 or 4 hours

Colchicine  $\frac{1}{8}$  gr, extract of hyoscyamus  $\frac{1}{2}$  gr, extract of nux vomica  $\frac{1}{2}$  gr, lactose  $\frac{1}{2}$  gr. Rapidly relieves gout

**[P1 81] Colchicine Salicylate.**  $C_{21}H_{19}NO_6, C_6H_5OH COOH = 537.2$ 

Dose.— $\frac{1}{160}$  to  $\frac{1}{80}$  grain (0.0005 to 0.002 g)

A yellowish powder soluble in water, alcohol and ether.

**[P1] Capsules** contain  $\frac{1}{160}$  gr in methyl salicylate Used in rheumatism and gout Dose —1 every 2 hours

**[P1] Colchi-Sal (Huxley Brand) Capsules.** (*Anglo-American Pharmaceutical Co., Croydon*) See Vol. II

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**COLLOIDS**

By the term "colloid" is meant a certain condition of matter depending chiefly upon the size of the particles. Thus a **Colloidal Solution**, or more correctly a colloidal sol, is a system wherein a solid or liquid is dispersed in a liquid medium, the size of the dispersed particles lying between 100 and  $1\mu\mu$ . When the disperse phase is a solid, it is called a suspensoid sol, and when a liquid, an

emulsoid sol. Thus the conditions are different from those in an ordinary solution where the solute is present either as molecules or ions or a mixture of the two. Unlike solutions, colloidal sols possess the following properties:—

#### Electrical Properties.

The disperse particles are charged positively or negatively. On passing an electric current through the sol, the positively charged particles move towards the cathode and the negatively charged towards the anode. This movement of particles in an electric field is known as *Kataphoresis*. On the addition of electrolytes, a suspensoid sol becomes unstable owing to the neutralisation of the charge, and the dispersed particles aggregate together and precipitate as larger particles. Precipitation or coagulation of a negatively charged sol is brought about mainly by the positive ion of the electrolyte and *vice versa*. Emulsoid sols are not readily precipitated by electrolytes. When an emulsoid sol is mixed with a suspensoid sol, the emulsoid particles appear to be adsorbed on to the surface of the suspensoid particles, with the result that the mixture is much more stable towards electrolytes. This fact is made use of in the preparation of colloidal metal sols which, alone, are typical suspensoid sols. A trace of added emulsoid sol, such as gelatin, agar, egg albumin, isinglass or acacia, confers stability on the preparation. The power to confer stability varies with those substances, and the value known as the *Zsigmondy Gold Number* is an expression of it. This is the number of milligrammes of colloid which, when added to 10 ml. of a gold sol containing 0.0053 to 0.0058% of gold, just protects the gold sol from a change of colour of red to violet when 1 ml. of a 10% solution of sodium chloride is added. The following are gold number values:—

	Gold Number.
Gelatin	0.005—0.01
Casein	0.01
Egg albumin	0.01—0.2
Acacia	0.15—0.25
Tragacanth	2.0—2.5
Dextrin	6.0—12.0
Potato Starch	25

It should be noted that the smaller the gold number the greater the protective power of the colloid.

Colloids such as gelatin are known as protective colloids. Amongst the sols having positively charged particles are the hydroxides of iron, aluminium and chromium, also the basic dyes such as methylene blue, methyl violet, etc. Negatively charged colloidal sols include those of metals, sulphur, iodine, soap and such acid dyes as congo red, eosin, indigo, fuchsine and resinous sols such as mastic, ginger, podophyllin, guaiacum, etc.

#### Osmotic Pressure.

The osmotic pressure of most colloidal sols is very small.

#### Brownian Movement.

The dispersed particles in a colloidal sol are in rapid motion, the phenomenon being known as the Brownian Movement. It may be observed in certain fine suspensions (not colloidal) using an ordinary microscope, but in colloidal sols it can only be detected by an ultramicroscope. The presence of Brownian Movement serves to distinguish a colloidal sol from a true solution which does not exhibit it. The movement is caused by the bombardment of the disperse particles by the molecules of the continuous phase.

#### Tyndall Cone.

When a parallel beam of light is passed through a colloidal sol, the path of the beam is visible. This again serves to distinguish a sol from a true solution, which does not show this phenomenon. A very similar phenomenon, due to fluorescence, is exhibited by some solutions, but whereas the beam of light made visible by the colloidal particles is polarised, this is not so in the case of fluorescence.

#### Isoelectric Point.

Many emulsoid sols, particularly those of amphoteric nature such as proteins, have varying charges on their particles according to the pH of the medium. At an intermediate point, the particles are uncharged. This point is known as the isoelectric point of the colloid, and is usually stated in terms of the pH.

of the medium. Colloids usually exhibit special physical properties at their isoelectric point, one being that of minimum solubility. This fact is often utilised in their separation from other colloids. Thus insulin is precipitated more easily at the isoelectric point, which lies between pH 5 and pH 6, than at other hydrogen ion concentrations.

### Dialysis.

Graham's original conception of *colloids* as substances which will not dialyse through an animal membrane in contradistinction to *crystalloids* which will so dialyse, no longer holds good to-day. The type of membrane used in the dialysis and the dispersion medium or continuous phase are factors which determine the retention or passage of the disperse phase. Thus a copper ferrocyanide membrane will hold back particles of molecular size. The process of dialysis is, however, an important process in removing electrolytes from mixtures after their employment as precipitants of colloids. The most useful membrane for general use is transparent cellulose tissue (*e.g.*, Cellophane) in the form of "sausage skins." It may be so obtained in long lengths capable of holding quite large volumes of liquids. The dialysing surface may be considerably increased by arranging a "skin" of smaller diameter inside a large one, placing the whole system in running water, allowing water also to flow through the central "skin" and placing the mixture for dialysis in the space between the two skins after the manner of a double surface condenser.

### TERMS USED IN THE NOMENCLATURE OF COLLOIDS

#### Lyophile Colloids.

This term refers to colloids such as gelatin, acacia, etc., which can form a sol by the mere addition of solvent or continuous phase in contradistinction to *lyophobic colloids*, such as the metallic sols, which will not do so, but require special dispersion methods. When water is the continuous phase the terms *hydrophile* or *hydrophobe* are used respectively.

#### Colloidal Electrolytes.

Certain substances such as soaps undergo electrolysis in water similar to electrolytes, but one of the ions is a complex, consisting of aggregated molecules and ions. These latter aggregates are called *ionic "micelles,"* and form the colloidal particles of the system. Some colloids, like collodion, have a disperse phase which is neutral or uncharged.

#### Gels.

Emulsoid sols may be of two types, those which are simple dispersions of liquids such as oils, and others like gelatin sols and agar, in which the particles are very heavily hydrated. In dilute sols these particles are separate, but as the concentration rises they appear to go in together to form a reticulated or sponge-like mass throughout the continuous phase. In this condition the whole system sets to a semi-solid condition which is known as a *gel*.

### METHODS OF MANUFACTURE

Colloids are used quite considerably in therapeutics mainly as metallic or metalloid sols. The processes of manufacture vary very considerably, and many are the subject of patents. In the 19th Edition Vol. I, p. 365, details are given relative to the preparation of sols of aluminium hydroxide, arsenic, bismuth, gold, manganese, selenium, etc., to which reference may be made, and particulars regarding the composition of colloidal solutions of certain elements and compounds are given under individual drugs (*see Index*). The following are the usual methods employed.



1. *Dispersion by precipitation in the presence of a protective colloid.* The precipitation may be the result of reduction, double decomposition, hydrolysis, etc. The preparation of colloidal silver is typical of this method.

Dextrin 4 is dissolved in distilled water 100, and sodium hydroxide 4 is added. Silver nitrate 3 is dissolved in water 20. This latter solution is added to the alkaline dextrin solution with constant stirring. Colloidal silver is formed, which is then precipitated by adding alcohol. The precipitate is washed free from alkali with more alcohol and dried. It may be incorporated in a moist condition in a wool fat basis for use as a colloidal silver ointment.

This type of method may be used for the preparation of colloidal calomel, iodine, ferric hydroxide, bismuth, sulphur, selenium, manganese and lead.

2. *Electrical Dispersion.* This method may be used for the preparation of metallic sols, particularly those intended for oral or parenteral administration. Electrodes made of the metal to be dispersed are immersed below distilled water, and so arranged as to produce a uniform arc when using a current of 8 amperes at about 110 volts. A small quantity of some protective colloid, such as gelatin, is added, the current switched on, and the arc maintained until the necessary concentration of dispersed metal is reached. This type of method is employed for the preparation of gold, silver and lead sols.

3. *Grinding.* Very fine dispersion may be obtained by a process of wet grinding in so-called colloid mills, although the particles are rarely within the colloid range of sizes. The method is used in the preparation of so-called colloidal calamine, sulphur and silver. It is possible, using an Agrex Mill, to reduce silver to particles of  $0.01\ \mu$ , which is within colloidal size. The machine works at 18,000 R.P.M. and is only suitable for large-scale production.

4. *Kataphoresis.* In the preparation of certain colloids such as kaolin, the material is first ground to approximate colloidal dimensions in a mill and some electrolyte such as sodium silicate is added. The silicate ions become adsorbed on the kaolin particles and, on providing an electric field, they move to, and are deposited at the anode.

#### THERAPEUTIC PROPERTIES OF COLLOIDS

The value of colloids in therapeutics has been the subject of much controversy. Special properties are claimed for them because of the very small size of the particles in comparison with an ordinary suspension or emulsion. This greatly reduced size confers a greatly increased specific surface and surface energy, and therefore greater activity. Where it is intended that a medication shall pass through the skin or have a local skin reaction, then the use of colloidal medicaments as ointments and lotions, etc., may have a justification. Similarly in the use of adsorbents

such as kaolin and charcoal in the treatment of alimentary toxæmia, it is logical to presume that a greater adsorption of toxins, etc., would occur if the size of the particles were of colloidal dimensions. It is, however, difficult to understand how a colloidal sol administered by the mouth can avoid being quickly coagulated thus ceasing to possess a special value. Moreover, because of the use of a protective colloid in a suspensoid sol, it is difficult to assess the value of the preparation. Its action may depend upon the protective colloid present, and may change when a different one is used. This is particularly so when such sols are administered parenterally, the reaction which follows being often due to the non-specific protein of the protective colloid. Moreover, many of the so-called suspensoid sols are not permanent, for the dispersed medicament reacts with the protective colloid to form another entirely different substance. This applies especially in the case of the so-called iodine sols.

Colloidal solutions are supplied commercially under the names **Collobell** (*John Bell, Hills & Lucas, London*), **Collosol** (*British Colloids, London*), **Oscol** (*Oppenheimer, Son & Co., London*). Colloidal solutions are also prepared by most manufacturing chemists.

## COLOCYNTHIS

*B P.*

*Syn* COLOCYNTHIDIS PULPA, COLOCYNTH PULP, BITTER APPLE, COLOQUINTIDE, COCOMERO AMARO (*P. Ital V*)

*Dose* —2 to 5 grains (0.12 to 0.3 g.). *P. Helv V* max single dose 5 grains, max. per day 15 grains. A teaspoonful and a half has proved fatal.

The dried pulp of the fruit of *Citrullus Colocynthis* (Cucurbitaceæ) containing not more than 5% of seeds, and not more than 2% of the outer sclerenchymatous part of the pericarp. Has a markedly bitter taste, is free from starch, and contains only about 3% of fixed oil or less, whereas the seeds contain 15% or more. Is imported from Smyrna (the best) and Spain.

**Antidotes.** Empty stomach by emetics or by stomach tube, using dilute tannic acid solution and leaving some in the stomach. Keep patient warm and give demulcent drinks freely. Stimulants, e.g., brandy,  $\frac{1}{2}$  oz., or aromatic spirit of ammonia,  $\frac{1}{2}$  dr., in water. Opium (tincture) by mouth or by rectum. Saline infusion if necessary.

**Uses.** A drastic cathartic. A frequent ingredient of aperient pills.

**Extractum Colocynthidis Compositum** (*B P*).

*Dose.*—2 to 8 grains (0.12 to 0.5 g.).

This is in powder form, made by extraction of colocynth and adding finely powdered aloes, scammony resin, curd soap and cardamom.

**Pilulæ Colocynthis Compositæ (B.P.C.).** *Syn.* PIL. COCHIA.

*Dose.*—1 or 2 pills.

Each pill contains colocynth  $\frac{3}{4}$  gr., aloes and scammony resin, of each  $1\frac{1}{2}$  gr., with curd soap and oil of clove.

**Pilulæ Colocynthis et Hydrargyri (B.P.C.)**

*Dose.*—1 or 2 pills.

Each pill contains compound extract of colocynth 2 gr. and pill of mercury 3 gr.

[P1] **Pilulæ Colocynthis et Hydrargyri Compositæ (B.P.C.).**

*Dose.*—1 to 4 pills.

Each pill contains pill of colocynth and hyoscyamus  $\frac{3}{4}$  gr. and pill of mercury  $\frac{1}{4}$  gr.

[P1] **Pilula Colocynthis et Hyoscyami (B.P.).**

*Dose.*—4 to 8 grains (0.2 to 0.5 g.).

Contains colocynth, aloes, scammony resin, curd soap, dry extract of hyoscyamus, and oil of clove with syrup of liquid glucose.

[P1] **Pulvis pro Pilula Colocynthis et Hyoscyami** consists of the ingredients of the pill less the syrup of liquid glucose. Is more convenient for dispensing.

[P1] **Hamilton's Pill.**

Compound extract of colocynth 2, extract of hyoscyamus 1, made into 4-grain pills. Stated to be less griping than the preceding.

[P1] **Pilulæ Hydrargyri Subchloridi, Colocynthis et Hyoscyami (B.P.C.).** *Syn.* ZITTMANN'S PILLS.

*Dose.*—1 or 2 pills

Each pill contains mercurous chloride 1 gr., compound extract of colocynth  $2\frac{1}{2}$  gr., dry extract of hyoscyamus 1 gr.

**Pilulæ Hydrargyri Subchloridi et Colocynthis (B.P.C.).**

*Dose.*—1 pill.

Each pill contains compound extract of colocynth 4 gr. and mercurous chloride 1 gr.

**Tinctura Colocynthis (P G. VI)**

*Dose.*—3 to 15 minims (0.2 to 1 ml). Maximum single dose 1 g; maximum daily dose 3 g

1 in 10 of alcohol (90%). *P. Ital V* is also 1 in 10 using 80% alcohol.

**Colocynthin.**  $C_{15}H_{14}O_{11} = 1124.7$ . The active principle, a glycoside, of colocynth in the form of an amorphous yellow powder. Has been employed as a hypodermic purgative.

*Dose*—15 minims of a 1% solution in glycerin, approximately  $\frac{1}{4}$  gr.

It occurs to the extent of 0.6%. It readily reduces Fehling's Solution.

[P1] **Elaterium (B.P.C.).** *Dose*— $\frac{1}{10}$  to  $\frac{1}{2}$  grain (0.006 to 0.03 g.), usually in pills.

The dried sediment from the juice of the nearly ripe fruit of *Ecballium Elaterium* (Cucurbitacæ). A powerful hydragogue cathartic, useful in renal or cardiac disease complicated with dropsy.

[P1] **Pilula Elaterii Composita (St. B.H.).** Elaterium  $\frac{1}{2}$  gr., compound extract of colocynth 2 gr., calomel  $1\frac{1}{2}$  gr., capsicum  $\frac{1}{2}$  gr.

[P1] **Tinctura Elaterii Composita.** *Dose*—10 to 30 minims

Elaterium in powder 1, chloroform 50, macerate 2 days, then add alcohol (90%) 200 and compound tincture of cardamom 250, macerate 5 days more and filter. Is more active than a corresponding dose of the powder.

[P1] **Elaterinum** (B.P.C.). *Syn.* MOMORDICIN.  $C_{28}H_{48}O_7$ . *Dose.*— $\frac{1}{4}$  to  $\frac{1}{10}$  grain (0.0015 to 0.006 g.). The crystalline neutral active principle (to extent of at least 20%) of elaterium, insoluble in water, soluble in chloroform (about 1 in 12) and sparingly in alcohol.

[P1] **Pulvis Elaterini Compositus** (B.P. 1898). *Dose*—1 to 4 grains Elatern 1, lactose 39.

## COLOPHONIUM

*B.P., U.S.P. XI, P. Helv. V, P. Dan.*

*Syn.* RESIN, ROSIN.

The residue after distilling the volatile oil (oil of turpentine) from the oleoresin of species of *Pinus*. **Soluble** in alcohol 90%, ether, benzene, carbon disulphide, and light petroleum.

**Ceratum Resinæ** (U.S.P. XI).

Resin 35, beeswax 15, lard 50

**Heusner's Glue.** Resin (commercial) 50, Venice turpentine 5, methylated spirit 50, benzene 25. For applying extension in fractures

The following have also been suggested—

(1) Dammar 250, castor oil or linseed oil 30, benzene 700, sodium bicarbonate 50, amyl acetate a few drops

(2) Colophony 300, Venice turpentine 20, castor or linseed oil 10, benzene 700, sodium bicarbonate 60, amyl acetate a few drops. *See also Brit. med. J.*, 1/1925, 441, and Mencièrè's solutions

**Spiritus Adhesivus Resinosus** (P. Svec. X) Terebinthina (i.e., common frankincense from *Pinus* var. esp. *P. pinaster*) 75, colophony 185, alcohol (90%) 4

**Unguentum Colophonil** (B.P.C.). *Syn.* UNGUENTUM RESINÆ, YELLOW BASILICON OINTMENT.

Colophony 26%, with yellow beeswax, lard and olive oil

**Copal** (B.P.C.). *Syn.* GUM ANIMI.

A fossil resin from *Trachylobium Hornemanianum* (Leguminosæ), occurring in pale yellow to reddish masses, entirely soluble in alcohol, partially soluble in benzene, glacial acetic acid, ether, chloroform and oil of turpentine. It is used in the manufacture of varnishes.

This is Zanzibar copal. Indian copal is from *Vateria indica* (Dipterocarpaceæ), and Brazilian is from *Hymenæa* species and other plants. Australian copal is Gum Kauri, *q.v.*

**Æther Copalis** (R.D.H.) (Copal Solution). Copal 1, ether 1, dissolve. For covering cement fillings to protect from the saliva

**Dammar** as used in this country for varnish making and for microscopical work is the East Indian Dammar from various species of *Shorea*, *Hopea* and *Balanocarpus* (Dipterocarpaceæ). It occurs in small yellow nodules, about 3 to 6 mm. in diameter. It is partially soluble in alcohol and soluble in chloroform.

**Kauri Gum.** A resin obtained from *Dammara Australis* in Australia and New Zealand. **Dental Compo** contains kauri gum. This is used for taking impressions when making dentures.

**Lacca** (B.P.C.). **SHELLAC.** A resinous substance formed by a scale insect, *Tachardia lacca* (fam. Coccidæ, ord. Hemiptera), which lives on a variety of trees, e.g., *Butea frondosa*, *Ficus religiosa*, *Schleichera tryuga*, *Shorea robusta* (Wild Lac). The plants specially cultivated for lac are *Acacia arabica* and *Cayanus indicus*. An ammoniacal solution has been used for the enteric coating of pills, capsules, etc.

**Mastiche** (*B.P.C., P. Helv. V, P. Dan., P. Belg.*). *Syn.* MASTIC  
*Dose.*— $\frac{1}{4}$  to  $\frac{3}{4}$  drachm (1 to 3 g.).

A resinous exudation obtained by puncturing the bark of *Pistacia Lentiscus* (Anacardiaceæ). In small, hard yellowish tears becoming plastic when chewed

**Insoluble** in water, partly soluble in alcohol 90%, also soluble 2 in 1 of ether and 2 in 1 of chloroform, readily in acetone.

**Alcohol Mastichi** (*R.D.H.*) Mastic 2, alcohol 90% 1, dissolve. Harvard Liquid is similar, this is employed for covering a cotton-wool dressing so as to form a temporary dental covering, e.g., during the treatment of canals

**Benzo Mastiche** (*Martindale, London*) A solution of mastic in benzene (with other ingredients) for wounds and general surgical use

The temporary first-aid bandage, if any, is removed and the wound, even if blood-smearred, is painted straight away with a sufficient covering of the preparation, and then a dressing applied. Slight injuries may have a layer of sterile gauze first to draw off the wound secretion. Useful in burns and corrosions of the 2nd and 3rd degree, the whole area being painted over and covered with cotton wool

**Mastisol** (*Schubert, Berlin*) A compound solution of mastic for application to wounds, etc

**Microscopic Varnish.** Mastic  $\frac{1}{2}$  oz., caoutchouc 15 gr., chloroform 2 oz., macerate and filter.

[P2] **Tinctura Ammoniae Composita** (*B.P.C.*) *Syn.* EAU DE LUCE

Contains 1  $\frac{1}{4}$ % of mastic with oil of lavender, alcohol 90% and strong solution of ammonia

**Sandaraca** (*B.P.C.*) *Syn.* SANDARAC, GUM JUNIPER. A resin obtained by incision from the stem of *Tetradlepis articulata* (Cupressaceæ). Brittle, pale yellow tears which do not agglomerate when chewed. Used in pill varnishes

**Sanguis Draconis** (*B.P.C.*) *Syn.* DRAGON'S BLOOD. A resinous secretion on the fruits of *Dæmonorops propinquus* and other species (Palma). In dull red pieces or lumps weighing up to several pounds. Used for colouring varnishes and in zinc line engraving to protect those parts not to be etched

**Oleum Succini** (*B.P.C.*) *Syn.* OIL OF AMBER, OLFUM SUCCINI RECTIFICATUM

*Dose.*—1 to 3 minims (0.06 to 0.2 ml.)

A yellowish liquid with penetrating odour obtained by the destructive distillation of resins, or by distilling resin oil. Has been given on sugar for asthma and whooping-cough. Used in liniments for its rubefacient properties

**Linimentum Succini Compositum** (*B.P.C.*) Oil of amber and oil of clove 25% v/v of each in olive oil

## CONIUM

[P1] "Alkaloids, the following; their salts, simple or complex—*Conine*"

[S1] "Alkaloids, the following; their salts, simple or complex—*Conine* except substances containing less than 0.1% of *conine*"

[P1 S1] **Conium Folium** (*B.P.C.*) *Syn.* HEMLOCK LEAF.

*Dose.*—2 to 8 grains (0.12 to 0.5 g.).

The fresh leafy tops of *Conium maculatum* (Umbelliferae). The leaves contain about 0.2% of total alkaloids chiefly *conine*.

**Incompatibility.** Conium preparations are incompatible with alkalis and preparations containing tannin.

**Antidotes.** Empty stomach by emetic or by stomach tube, using dilute tannic acid solution. Leave some tannic acid in the stomach as an antidote, or give medicinal charcoal, stirred up in water. Keep patient lying down and warm. Artificial respiration and oxygen with 7% carbon dioxide inhalations may be necessary. Stimulants, *e.g.*, brandy  $\frac{1}{2}$  oz, or aromatic spirit of ammonia,  $\frac{1}{2}$  dr, in water. Strychnine,  $\frac{1}{8}$  gr, or caffeine sodium benzoate, 2 gr, hypodermically.

**Uses.**—Conium and coniine hydrobromide act as direct sedatives to the respiratory centre; in poisonous doses death is caused by asphyxia. Employed with advantage in all spasmodic affections, especially for whooping-cough and asthma; in neuralgia, epilepsy, and as a sedative in acute mania.

[P1 81] **Extractum Conii** (B P C) Dose —2 to 6 grains (0.12 to 0.4 g)

A soft extract prepared from the expressed juice

[P1 81] **Succus Conii** (B P C) Dose — $\frac{1}{2}$  to 1 drachm (2 to 4 ml)

The expressed juice preserved with alcohol

[P1] **Unguentum Conii** (B P C) Syn HEMLOCK OINTMENT

Extract of conium 7%, in glycerin and simple ointment. Gives relief in pruritus ani and painful fissures.

[P1 81] **Conii Fructus** consists of the dried unripe fruits and contains up to about 2.5% of total alkaloids mainly coniine.

[P1 81] **Tinctura Conii.** Dose — $\frac{1}{2}$  to 1 drachm (2 to 4 ml)

Conium fruit, No. 40 powder, 1 in 5 of alcohol 60%, prepared by percolation, and standardised to 0.1% of coniine.

[P1 81] **Extractum Conii Liquidum.** Dose —5 to 15 minims (0.3 to 1 ml).

Conium fruit 100, in No. 40 powder, is exhausted with alcohol 60% containing 1.25% of acetic acid (33%), the last portion of percolate concentrated and mixed with the first 85 previously set aside, so as to produce a liquid extract containing alkaloids equivalent to 1% of alkaloidal hydrochlorides.

[P1 81] **Extractum Conii Fructus.** Syn EXTRAIT DE CIGUE (Fr. Cx) Dose —Maximum single  $\frac{1}{2}$  grain (0.05 g), approximately, but up to 2 grains are often given—as in Pil. Antim. Conii et Quininae.

A firm extract produced by extracting the powdered fruits with 70% alcohol at 35°, evaporating the liquor and treating the residual extract with water, evaporating the aqueous extractive, rejecting the portion not dissolved.

[P1 81] **Coniina.** Syn. CONINE, CICUTINE, *d*- $\alpha$ -PROPYLPYPERIDINE  
 $C_8H_{10}N(C_7H_7) = 127.1$

Dose — $\frac{1}{16}$  to  $\frac{1}{8}$  grain (0.001 to 0.01 g)

An almost colourless liquid with mouse-like odour and acrid taste. B.p. about 166°. **Soluble** 1 in 100 of water, and in organic solvents.

[P1 81] **Pessus Coninae.** Coniine  $\frac{1}{2}$  m., gelatin mass 20 gr

[P1 81] **Coniinae Hydrobromidum** (B P C, Fr. Cx).

$C_8H_{17}N, HBr = 208.1$  Syn CICUTINÆ BROMHYDRAS (F E VIII).

Dose.— $\frac{1}{16}$  to  $\frac{1}{8}$  grain (0.004 to 0.016 g.).

F.E. specifies single dose  $\frac{1}{16}$  grain (0.001 g.); during 24 hours,  $\frac{1}{16}$  to  $\frac{1}{8}$  grain (0.005 to 0.02 g.). Fr. Cx. has max. single dose  $\frac{1}{8}$  gr, max. in 24 hours 2 $\frac{1}{2}$  gr approx.

Colourless crystalline prisms **soluble** 1 in 2 of water and 1 in 3 of alcohol 90%.

[P1·81] **Injectio Conilinae Hydrobromidi.** Dose.—1 to 3 minims (0·06 to 0·2 ml.). 1 gr. in 20 m.

**Eranthe Crocata** (Umbelliferae) Water dropwort—the most dangerous and virulently poisonous of all British native plants. It contains no alkaloid. Contains a yellow essential oil with unpleasant odour and a viscid resin, nearly 3%, giving rise to convulsions by acting on the spinal medulla. The stem has poisoned children, being mistaken for Angelica. The roots resemble parsnip and are not unpleasant to the taste.

**Eranthe Fistulosa.** Syn. HEMLOCK DROPWORT Poisoning from, due to conium content —*Lancet*, 1/1931, 1309.

**Scoparium** (B.P.C.) Syn. BROOM TOPS, SCOPARII CACUMINA

The fresh or dried tops of *Cytisus scoparius* (Leguminosae). Contains the alkaloids sparteine, genisteine and sarothamnine. Is mildly diuretic in cardiac dropsy.

**Decoctum Scoparii** (B.P.C.). Dose —2 to 4 ounces (60 to 120 ml.) 1 in 20

**Decoctum Scoparii Concentratum** (B.P.C.). Dose —2 to 4 drachms (8 to 16 ml.) 1 in 2½ Is eight times the strength of the fresh decoction

**Infusum Scoparii Concentratum** (B.P.C.). Dose —1 to 2 drachms (4 to 8 ml.) 1 in 1½ Is eight times the strength of the fresh infusion.

**Infusum Scoparii Recens** (B.P.C.). Dose —1 to 2 ounces (30 to 60 ml.) 1 in 10

**Succus Scoparii** (B.P.C.). Dose —1 to 2 drachms (4 to 8 ml.). The juice expressed from the fresh plant, preserved with alcohol

**Scoparin**,  $C_{15}H_{11}O_{11}$ , a phenolic body in broom tops. Has definite diuretic action in doses of 5 to 8 grains.—*Chem. & Drugg*, 1/1930, 58.

**Sparteina**.  $C_{15}H_{25}N_2$ . A volatile liquid alkaloid obtained from broom. Is colourless when fresh, darkening on keeping. Sparingly soluble in water, soluble in alcohol 90%, chloroform and ether.

The pharmacological action of sparteine and related alkaloids —R St A Heathcote, *J. Pharmacol*, June, 1926, 431.

**Sparteinae Sulphas** (B.P.C., Fr. Cx., P. Helv V)

$C_{15}H_{25}N_2 \cdot H_2SO_4 \cdot 5H_2O = 422\cdot4$  Dose —1 to 2 grains (0·06 to 0·12 g.). Fr. Cx. has max. single dose ¾ grain, max. during 24 hours 4 grains.

In colourless crystals. **Soluble** 2 in 1 of water, and about 1 in 5 of alcohol 90%.

**Uses.** Much less poisonous than conium but similar in action. Resembles digitalis in its action on the heart and is of value in myocardial degeneration. The effect is cumulative owing to slow excretion. With potassium iodide is given in hypertension. It has a marked diuretic action, probably acting through the heart, and is effective in dropsy and post-operative retention of urine. Has been used as a sedative in the withdrawal treatment of opium and morphine addiction.

**Viscum** (B.P.C.). Syn. MISTLETOE Dose —10 to 60 grains (0·6 to 4 g.). The whole plant, *V. album*, growing as a semi-parasite on various trees, especially the apple, poplar and plum. Has vasodilator action and is used in high blood pressure; has also been used in hysteria and chorea. Administered as a soft extract in pills or as infusion, tincture or liquid extract.

In albuminuria said to be of value. Solid extract used, 0.1 to 0.3 g. *per diem*; acting best when blood pressure and tension are high.

Hyperpiesia treated by extract of viscum injections intramuscularly (0.05 g. night and morning) and *per os* in pills (0.15 g. night and morning) — *Brit. med. J. Ept*, 11/1926, 17.

**Detensyl** (*Continental Laboratories, London*). Mistletoe, liver, pancreas and lung Tablets for use in hypertension and disorders of the menopause

**Guipsine** (*Leprince, Paris; Bengué, London*). Pills stated to contain 0.05 g. of active principles of this drug Fresh mistletoe contains a volatile alkaloid and two saponins and emetic and cathartic resin. Guipsine is stated to contain all these excepting the resins It lowers arterial tension due to a central vasomotor action, and is without any depressing action on the heart itself For use in arteriosclerosis. *Dose* — 4 to 10 daily.

**Hypotensyl** (*Anglo-French Drug Co, London*) Viscum album extract 0.075 g., hepatic extract 0.10 g., pancreatic extract 0.05 g.

*Dose*. — 3 to 6 tablets daily for continuous periods of 15 to 20 days with a week's interval between courses. Hyperpiesia

## COPAIBA

*B P, U.S.P. XI, P. Helv V, P Dan., etc.*

*Syn.* BALSAMUM COPAIVÆ, BALSAM OF COPAIBA.

*Dose*. — 10 to 30 minims (0.6 to 2 ml)

The oleoresin obtained from the trunk of *Copaifera Lansdorfii* and other species (*Leguminosæ*), imported from the coast of South America

**Soluble** almost completely 1 in 1 of alcohol 90%; miscible with dehydrated alcohol, ether, carbon disulphide, fixed and volatile oils. Soluble in an equal volume of light petroleum (b. p. 50° to 60°) but precipitated on adding more solvent. That known as Para copaiba is transparent, yellowish and contains 60 to 90% of oil It is thinner than the Maracaibo variety, which is brownish and somewhat fluorescent and contains about 45% of oil. Sp. gr. about 0.960 to 0.995.

**Uses.** Diuretic and stimulant to mucous membranes, chiefly used for urethral diseases, and occasionally for chronic bronchitis May produce a red rash. Given emulsified with mucilage or saponified, but best in capsule

**Oleum Copaibæ** (*B.P.C.*).

*Dose*. — 5 to 20 minims (0.3 to 1.2 ml.).

Distilled from the oleoresin. Sp. gr. 0.896 to 0.910.

**Soluble** in its own volume of dehydrated alcohol and about 1 in 20 of alcohol 90%.

Is used for the same purposes as copaiba.

[P1] **Hausustus Copaibæ** (*St. G. H.*).

Copaiba 15 m., tincture of hyoscyamus 30 m., sodium citrate 30 m., mucilage of acacia 1 dr., peppermint water to 1 oz.

**Liquor Copaibæ** (*B.P.C.*). *Syn.* SOLUBLE COPAIBA.

*Dose*. — 1 to 2 drachms (4 to 8 ml), well diluted.

Copaiba 50% dissolved in a potassium hydroxide solution,



**Liquor Copaibæ, Buchu et Cubebæ (B.P.C.)**

*Dose*.—1 to 2 drachms (4 to 8 ml) well diluted.

Solution of copaiba 80% v/v with liquid extracts of buchu and cubeb

**Liquor Copaibæ, Buchu et Cubebæ cum Oleo Santali (B.P.C.)**

*Dose*—1 to 2 drachms (4 to 8 ml)

Resembles the preceding solution but contains also 10% v/v of oil of sandal wood and 5% v/v of oil of cassia

**Liquor Copaibæ et Olei Santali (B.P.C.)**

*Dose*—1 to 2 drachms (4 to 8 ml)

Contains 80% v/v of solution of copaiba with oils of sandal wood and cassia

**[P1] Mist. Copaibæ (N.I.F.)**

Copaiba 15 m, solution of potassium hydroxide 15 m, tincture of hyoscyamus 15 m, infusion of buchu to  $\frac{1}{2}$  oz

**African Copaiba** is obtained from an unknown botanical source. It is a dark yellow fluorescent oleoresin containing 40% of oil

**Cubeba (B.P.C.).** *Syn* TAILED PEPPER *Dose*.— $\frac{1}{2}$  to 1 drachm (2 to 4 g.) in cachets.

The dried unripe full-grown fruit of *Piper Cubeba* (Piperaceæ) imported from Java. Contains 10 to 18% of volatile oil. It is sometimes added to Ferrier's snuff, *q.v.*

**Cubeb Cigarettes** are useful for catarrh and excessive bronchial secretion.

**Extractum Cubebæ Liquidum (B.P.C.)** *Dose*— $\frac{1}{2}$  to 1 drachm (2 to 4 ml) 1 in 1

**Oleoresina Cubebæ (B.P.C.)** *Dose*—5 to 30 minims (0.3 to 2 ml)  
The ether-soluble extractive

**Tinctura Cubebæ (B.P.C.)** *Dose*— $\frac{1}{2}$  to 1 drachm (2 to 4 ml)  
1 in 5 of alcohol (90%). In chronic bronchitis as an expectorant

**Trochisci Cubebæ (T.H.)** contain  $\frac{1}{2}$  gr. each with fruit paste *Dose*—1 every 3 or 4 hours

**Oleum Cubebæ (B.P.C., P. Helv. V.)** *Dose*—5 to 20 minims (0.3 to 1.2 ml)  
Colourless, pale green or greenish yellow oil, with camphoraceous odour and characteristic taste. Soluble about 1 in 18 of alcohol 90%. **Capsules** contain 10 minims. For combinations *cf.* **Oleum Santali**. Used in bladder and urethral affections, also as an inhalation in bronchitis

**Vapor Cubebæ cum Limone (T.H.)**

Oil of cubeb 40 m, oil of lemon 10 m, light magnesium carbonate 20 gr, water to 1 oz. A stimulant inhalation

**Oleum Santali (B.P., U.S.P. XI, P. Helv. V.)**

*Dose*.—5 to 15 minims (0.3 to 1 ml.)

Santal or sandal wood oil is distilled by steam under pressure from the wood of *Santalum album* (Santalaceæ), the yield being from 1 to 6%. A yellowish oil, with an aromatic odour and pungent taste

**Soluble** 1 in less than 1 of alcohol 90%, also in ether and chloroform

**Uses.** Internally in chronic bronchitis, *e.g.*, a few drops taken on a lump of sugar is found to relieve cough without expectoration. Is much employed in the treatment of gonorrhœa and gleet. It quickly checks the discharge in dose of 15 minims 3 times a day, and with the use of permanganate, zinc and silver nitrate injections gives good results, also in 10 minim capsules, with benzoic and boric acids as adjuvants, for chronic cystitis.

Urinary infections due to the staphylococcus. The oil has an almost magical effect.—W. K. Irwin, *Brit med J.*, ii/1925, 37.

**Mistura Olei Santali.** *Dose.*—1 ounce (30 ml)

Oil of sandal wood 4, tragacanth, in powder, 1 Mix and add quickly water to 128 Shake well Aromatic water with syrup may be used

**Mistura Santali Composita.** *Syn* NISBET'S SPECIFIC.

*Dose* — $\frac{1}{2}$  to 1 drachm (2 to 4 ml) in water or milk thrice daily

Santal oil 12 $\frac{1}{2}$  dr, cassia oil 1 $\frac{1}{2}$  dr, pimento oil 40 m, alcohol (90%) 3 $\frac{1}{2}$  oz

**Capsules of Nisbet's Specific** are prepared containing the oils of  $\frac{1}{2}$  drachm dose of the above in 20-minim capsules

**Liquor Santali cum Buchu et Cubeba.**

*Dose* —1 to 2 drachms (4 to 8 ml) well diluted

Yellow santal wood in powder 4, buchu in powder 1, cubeb in powder 1, alcohol 60% q s to moisten Macerate 2 days, percolate with more alcohol and press to obtain 20

**Liquor Santali Compositus (B P C)**

*Dose* —1 to 2 drachms (4 to 8 ml) diluted

Oil of sandal wood 5% with tincture of cubeb, tincture of buchu, and oil of cinnamon in alcohol 90%.

**Oleum Santali Australiensis (B P).**

*Dose* —5 to 15 minims (0.3 to 1 ml) Australian sandal wood oil is derived from *Eucarya spicata* and is largely used in Australia and other countries It contains alcohols equivalent to not less than 90% w/w calculated as  $C_{15}H_{24}O$  This oil might replace the more expensive oil from *S. album*.

**Eumictine (Bengué, London)** Santalol, salol and hexamine *Dose* —8 to 12 capsules daily with meals Gonorrhœa, cystitis, etc

**Gonosan (Riedel-de Haen, Berlin, Old Strand Chemical Co, London).**

Sandalwood oil 80%, kava-kava resin 20% Capsules contain 0.3 g

*Dose* —2 capsules 3 to 5 times a day Gonorrhœa

**Santal Midy (Laboratoire de Pharmacologie Générale, Paris; Phargène, London).** Capsules (0.25 g) of Mysore citrin sandalwood oil containing 92 to 95% santalol *Dose* —2 to 4 capsules 3 times a day before meals Urinary tract affections

**Santyl (Knoll, London, Pharmaceutical Products, London)** Salicylic ester of santalol *Dose* —25 to 50 drops of liquid thrice daily or 2 capsules (each 7 m) after food thrice daily Acute gonorrhœa and urinary affections.

**Savarese's Capsules (Evans, Sons, Lescher & Webb, Liverpool)** contain 10 minims of santalyl salicylate and are prepared with an animal membrane which generally remains entire until they have passed the stomach

**Sabal (B P C).** *Syn.* SAW PALMETTO.

*Dose* —15 grains (1 g).

The partly dried fruits of *Serenoa serrulata* (Palmæ). Reputed to have stimulant action on genito-urinary mucous membrane and used in gonorrhœa and cystitis

**Extractum Sabal Liquidum (B P C)** *Syn* LIQUID EXTRACT OF SAW PALMETTO *Dose* —10 to 25 minims (0.6 to 1.5 ml) 1 in 1.

**Sanmetto (Od Peacock Sultan Co, St Louis, U S A.)** is a preparation of sabal and santal for use in genito-urinary affections

**Kava (B P C).** *Syn* KAVA-KAVA, AWA ROOT.

The rhizome of *Piper methysticum* (Piperacæ) from the Polynesian Islands Used as diuretic and genito-urinary antiseptic In gonorrhœa it is not equal to copaiba or santal oil

**Extractum Kava Liquidum (B P C.)**

*Dose* — $\frac{1}{2}$  to 1 drachm (2 to 4 ml). 1 in 1

## CREOSOTUM

B.P., U.S.P. XI, P.G. VI, P. Ital. V, P. Belg. IV, P. Helv. V,  
P. Dan.

Syn. KREOSOTUM, CREASOTE.

[P1] "Creosote obtained from wood."

[83] "Creosote obtained from wood—in substances containing less than 50% of creosote obtained from wood."

**Dose.**—2 to 10 minims (0.12 to 0.6 ml.), increased to 30 or even 60 minims, in capsules, or in cod-liver, almond, or olive oil, or emulsified in oil with acacia. If ordered in aqueous mixtures in excess of solubility it may be suspended with mucilage of tragacanth or with tincture of quillaia.

Is a mixture of phenols—chiefly guaiacol and creosol. The variety most used is from beechwood. It contains a large percentage of guaiacol,  $C_6H_4 \cdot OCH_3 \cdot OH = 124.1$ . It mixes clear with glycerin. It is more soluble in water than the variety from pine-wood, which is anhydrous and mixes perfectly with oil of turpentine, consisting chiefly of creosol,  $C_6H_3 \cdot CH_3 \cdot OCH_3 \cdot OH : 1, 3, 4 = 138.1$ , homopyrocatechin-methyl-ether (Morson's creosote is representative of this class). Creosote does not cause collodion to gelatinise when mixed with it in equal proportion, provided the collodion is prepared with pyroxylin of the minimum viscosity specified in the B.P.

**Commercial creosote** used for timber preservation consists of naphthalene oils—a mixture of the heavy oil from coal tar distilling at  $230^\circ$  to  $270^\circ$ , with the residues from the middle oil ( $170^\circ$  to  $230^\circ$ ), after freeing from phenols.

**Soluble** about 1 in 150 of water; miscible with alcohol 90%, ether, and with fixed and volatile oils.

**Incompatible** with silver oxide (*q.v.*). Also with calcined magnesia and slaked lime.

**Antidotes.** Treat as for poisoning by carbolic acid, *see* p 745.

**Uses.** Locally as a caustic. It is one of the most powerful deodorisers, antiputrescents, and antiseptics. It is used internally to correct fetor, to check sickness, for diabetes, added to cod-liver oil for phthisis and applied externally in various skin diseases, and is put into the cavities of carious teeth. Internally it checks gastric fermentation and is an intestinal antiseptic in some forms of diarrhœa. For irritable trachea and congested larynx, causing troublesome cough, the inhalation of creosote from an oro-nasal or "ozonic" inhaler is useful. *Hypodermically* has been administered in 10% solution in almond oil.

**ACNE.**—Good results when given in doses of not less than 6 minims 3 times a day, but urine should be watched for toxic effects.—A. Whitfield, *Brit. J. Dermat.*, 1934, 257.

**PNEUMONIA.**—After a wash-out enema, inject slowly well up the rectum 40 drops of creosote shaken in 2 oz. of warm milk; retain for 2 hours. Repeat if not retained for more than  $\frac{1}{2}$  hour; in adults add 10 drops of tincture of opium. Repeat enema twice in 24 hours. For children under 1 year give 2 to 10 drops

and older children 5 to 10 drops, with extra drop for each year. Almost specific in pneumococcal conditions, prophylactic in post-operative pulmonary complications and clears up catarrhal states prior to operation—Ian Macdonald, *Brit med. J.*, 11/1931, 1111. Value queried.—H. Sutherland, *ibid*, 1198.

**Aqua Creosoti.** *Syn.* LIQUOR CREOSOTI. *Average dose.*—2 drachms. A freshly prepared aqueous solution of creosote 1 in 100

**Elixir Creosoti** (*Martindale*).

*Dose*—1 to 2 drachms (4 to 8 ml.) diluted at the time of taking.

Creosote 2 m., alcohol 90% 10 m., syrup of pine and simple elixir, equal parts to 2 dr.

**Mist. Creosot. c. Pot. Iod. (N I F).**

Creosote 2 m., potassium iodide 5 gr., tincture of quillaia 2½ m., liquid extract of liquorice 30 m., water to ½ oz

Expectorant, and given in phthisis Also valuable in lobar pneumonia The antiseptic action of creosote limits the extension of the pneumonic process

Doubtful whether its beneficial effects (in lobar pneumonia) are commensurate with its unpleasantness and its bad influence on appetite and digestion.—Price

**Nebula Creosoti Composita.** Creosote 5 minims, cassia oil 5 minims, almond oil to 1 ounce

**Pilula Creosoti** *Dose*—2 to 6 grains (0.12 to 0.4 g.).

Creosote 1, curd soap, in powder, 1, digested on a water-bath in a wide-mouthed stoppered bottle As prophylactic against dysentery

To make a pill containing creosote 2 m. and phenol 1 gr. use white wax 2½ gr and powdered liquorice 1 gr Incorporate the phenol, creosote and wax with the powder gently and quickly.

Perles of creosote, 1 or 3 minims in each, with oil, also capsules, 3 and 5 minims, or more, with oil are made.

[P1] **Creocarb Capsules.** Contain beechwood creosote 3 m. and phenol ½ gr in the treatment of phthisis.

**Spiritus Creosoti.**

*Dose*—1 drachm Creosote 1, alcohol 90% 40 Lessens cough and expectoration in chronic bronchitis and phthisis.

**Syrupus Creosoti Compositus (B.P.C.).**

*Dose.*—1 to 2 drachms (4 to 8 ml.).

Contains 1 minim of creosote per drachm with spirit of chloroform, glycerin, syrup, and syrup of pine.

**Unguentum Creosoti (B.P.C.)** contains 10% of creosote in a beeswax, lard and paraffin basis.

Used in psoriasis and parasitic skin diseases. *Caution.*—Should not be applied to the abdomen, face, or flexor surfaces of the limbs.

**Vapor Creosoti (T H).**

Creosote 80 m., French chalk 30 gr., water to 1 oz C L T.E. has creosote 40 m., light magnesium carbonate 20 gr., water to 1 oz

A teaspoonful (C L T.E. a tablespoonful) in a pint of water at 140°F. Useful in chronic congestion of the larynx and trachea, and in ozæna, fetor of breath and syphilitic throats For phthisis, it is more sedative in its action if mixed with an equal volume of spirit of chloroform, 5 to 20 m being employed at one time

[P1] **Famel Syrup** (*P. Famel, Paris, Wilcox, Jozeau, London*). Purified soluble creosote 1.00 g., calcium lactophosphate 0.50 g., codeine 0.025 g., alcoholat aconit (*Fr. Cx*) 0.50 g., syrup of lemon to 100.0 g *Dose*—A dessertspoonful twice a day well diluted with water. Coughs, colds, bronchitis, etc

**Calcii Creosotas (U.S.P. XI).**

*Dose.*—4 to 16 gr. (0.25 to 1 g.). U.S.P. XI average dose 8 gr., given every 2 to 4 hours, beginning with small doses and increasing gradually.

A mixture of the calcium compounds of the constituents of creosote, containing when dried 40 to 50% of CaO. A dark brown

powder with sharp phenolic taste Partially **soluble** in water, insoluble portion consisting of calcium hydroxide and carbonate

Used for administration of large quantities of creosote, but the increased tolerance is probably due to slower absorption and excretion Does not cause nausea and vomiting

**Calcreose** (*Maltbie Chemical Co., Newark, N.J.*) Preparations of calcium creosotate available as tablets (4 gr.), compound syrup, and solution

**Creosoti Carbonas** (*B.P.C., U.S.P. XI, P. Ned. V, F.E. VIII, P. Belg. IV, P. Helv. V.*) *Syn.* CREOSOTAL (*Heyden, Dresden; Braun, London*)

**Dose.**—5 to 20 minims (0.3 to 1.2 ml.) or considerably increased. *U.S.P. XI* average dose 15 grains. May be given in capsules or in milk

A colourless or amber-coloured nearly odourless syrupy liquid, sp. gr. 1.15 to 1.18. Soluble in alcohol, chloroform, ether, benzene and fixed and volatile oils, insoluble in water or glycerin

It contains the carbonates of guaiacol and creosol and decomposes in the alkaline intestinal juices. Has been used in tuberculosis, bronchitis and pneumonia.

**Proposote Capsules** (*Parke, Davis, London*) Contain 5 m. of creosote phenylpropionate **Dose**—1 capsule after each meal Tuberculosis, bronchitis, also in intestinal disorders of bacterial origin

**Guaiacol** (*B.P., U.S.P. XI*)

**Dose**—5 to 10 minims (0.3 to 0.6 ml.). *U.S.P. XI* average dose 8 minims.

Occurs in two forms, liquid and solid, both of which are recognised by *B.P.* and *U.S.P. XI*. The crystals are official in *P. Belg. IV, P. Ned. V, P. Ital. V* and *F.E. VIII*. The liquid is obtained by distillation of wood-tar creosote and consists mainly of *o*-dihydroxybenzene monomethyl ether,  $C_6H_4(OCH_3)OH = 124.1$  The crystals of the pure ether are obtained synthetically by heating catechol, potassium hydroxide and potassium methylsulphate. *M.p.* about 28°. No dose is given in *B.P.* for the solid. Both forms resemble creosote in taste and odour

**Soluble** 1 in 80 of water, miscible with alcohol 90%, ether, glycerin, and fixed and volatile oils

**Uses.**—In phthisis, particularly in incipient stages, may be prescribed in capsules (guaiacol carbonate), or cordial, *e.g.*, guaiacol 13.5, compound tincture of gentian 30, alcohol (90%) 250, and sherry to 1000; two teaspoonfuls two or three times a day in water—or as *Mistura Guaiacolis*, *vide postea* Antiseptic and antipyretic. It is sometimes rubbed into or painted on the skin, covered by oiled silk; begin with 10 minims and increase to 30 or more, do not cover more than the space of the palm of the hand at a time As a paint for infected tonsils guaiacol 3 dr. in olive oil to 1 oz. is of value.

**Injections** of guaiacol 5%, and iodoform 1%, in sterilised olive oil, in doses of 1 ml., increasing to 3 ml., have been used in tuberculosis, they are not free from danger and the drug is better given *per os*

**Durant's Injection.** Guaiacol 5, iodine 1, potassium iodide 10, sterile olive oil 100. In pulmonary phthisis

For tuberculous uveitis guaiacol has been extolled 1 ml of 1% solution injected, but these subconjunctival injections are not approved by all

**Injectio Guaiacolis Iodi et Camphoræ.**

*Dose*—4 minims (0.25 ml) intramuscularly, increased at three-day intervals to 15 minims (1 ml) and this repeated every 2nd or 3rd day

Contains guaiacol and iodine (in only combination as in iodinol) of each 10% and camphor 5%

Rheumatoid arthritis and articular fibrositis, other than the post-infective gouty and gonorrhœal forms, well treated—G. Watson Smith, *Brit med J*, 11/1925, 648

**Mistura Guaiacolis** *Dose*—½ ounce (15 ml) thrice daily

Guaiacol 1 dr, alcohol (90%) 1 oz, syrup of lemon 1 dr, spirit of chloroform 2 dr, water to 6 oz Increase guaiacol by 2 m each week until a dose of 12 to 15 m is given thrice daily, and continue for four months or more

**Mistura Guaiacolis cum Quinina.**

*Dose*—½ drachm gradually increased to 2 drachms, well diluted with water, thrice daily after meals

Guaiacol 30 to 40 m, quinine hydrochloride 20 to 25 gr, alcohol (90%) 2 oz compound tincture of gentian 3 oz, water to 8 oz The small dose of guaiacol thus given is increased by giving guaiacol carbonate in capsules

**Nebula Guaiacolis et Mentholis Composita (B P C)** Guaiacol and menthol, 2% w/v in light liquid paraffin

**Unguentum Guaiacolis.** Guaiacol 1, lanolin ointment (or other suitable basis) 5, useful in orchitis and mumps, and in tuberculosis

**Vapor Guaiacol Compositus**

Guaiacol and terebene of each 2, menthol and thymol of each 1, spirit of chloroform 3 Inhalc 5 to 10 minims from an inhaler night and morning Employed in phthisis

[D P I 81] **Fuller's Inhalant.**

Guaiacol 4, menthol 2 5, Sydenham's laudanum 125, compound tincture of benzoin to 250 Sometimes terebene 4 is added

**Bronchodermine (Bengué, London)** Guaiacol, terpinol, eucalyptol, heleninc, pine oil Applied to the back as a liniment in respiratory affections

**Quinacol (Allen & Hanburys, London)** Quinine with guaiacol in capsules. *Dose*—One capsule (4 m) increasing to 4 or 5, daily children one capsule (2 m) increasing to 3 or 4, daily Phthisis, whooping-cough, bronchitis, etc

**Guaiacolis Benzoas.**  $C_6H_4 OCH_3 O CO C_6H_5$  - 228.1

*Dose*—4 to 12 grains (0.25 to 0.8 g) in cachet

In small crystals, almost tasteless, nearly insoluble in water.

**Incompatible** with alkalis

Useful as an intestinal antiseptic and in incipient phthisis (especially for the diarrhœa)

**Guaiacolis Camphoræ.** *Syn* GUAICAMPHOL

$[C_6H_4 OCH_3 O]_2(CO)_2C_8H_{14}$  or  $C_{24}H_{28}O_6$  = 412.2.

*Dose*—5 to 10 grains (0.3 to 0.6 g) in cachets or 5-gram tablets

Soluble only very slightly in alcohol, insoluble in water, for night-sweats and diarrhœa of phthisis

**Guaiacol Carbonas (B P C and majority of pharmacopœias).**

$(C_6H_4 OCH_3 \cdot O)_2CO$  = 274.1

*Prop Name* DUOTAL (*Heyden, Dresden, Braun, London*)

*Dose*—5 to 15 grains (0.3 to 1 g), gradually increased

A white crystalline substance, almost tasteless, and with slight odour.

**Soluble** about 1 in 70 of alcohol 90%, and 1 in 20 of ether, readily in chloroform and in benzene; insoluble in water.

**Uses.**—In phthisis, improves appetite and lessens cough, expectoration and night sweats, also in typhoid and for bronchitis.

In rheumatoid arthritis, both the subacute and chronic forms, it sometimes arrests the disease, diminishes size and increases movement of joint and relieves pain. To be given in cachets thrice daily in gradually increasing doses until each dose is 15 to 20 grains—to be continued at least twelve months. At the same time a mixture containing 10 grains of potassium iodide in each dose to be given.

**Mistura Arthritica (C X H).**

Potassium iodide 5 gr., sodium salicylate 5 gr., sodium bicarbonate 5 gr., guaiacol carbonate 5 gr., mucilage of tragacanth 1 dr., chloroform water to 1 oz.

**Tabellæ Guaiacolis Carbonatis (B P C)** contain 5 gr. (0.3 g.).

**Guaiacolis Cinnamas.** Dose—5 to 15 grains (0.3 to 1 g.) White insoluble crystals, given in incipient phthisis

**Styracol (Knoll, London; Pharmaceutical Products, London)** Cinnamic ester of guaiacol Dose—1 or 2 tablets (7½ grains) thrice daily Catarrhal conditions of the respiratory tract.

**"Iodised Tincture of Guaiacol" (British Drug Houses, London).** Dose.—1 drachm twice daily. Used in pleurisy and synovitis of various types, neurosyphilis of the cerebrospinal system, meningitis, etc

**Tinct. Guaiacol Chlor-Iodide (British Drug Houses, London).** Syn. G.C.I. An internal antiseptic for treatment of boils, whitlows, tonsillitis, erysipelas, etc

**Guaiacolis Valerianas.** Dose—2 to 15 minims (0.12 to 1 ml.) A colourless liquid occasionally administered in capsules as an intestinal antiseptic

**Calcium Guaiacolsulphonate.** Syn. GUAIACYL. Dose.—10 minims (0.6 ml.) of 5% solution or 1 ml. of 10% solution subcutaneously Local anæsthetic

Has been employed intravenously, 0.33 g. in 20 ml., in tuberculosis and pulmonary affections. This dose is equivalent to ¼ grain of calcium and 3 grains of guaiacol.

Guaiacolsulphonic acid and its salts do not yield guaiacol in the system and they are therapeutically inactive—*Yearb. Pharm.*, 1924, 340

**Potassii Guaiacolsulphonas (B.P.C., Fr. Cx. Supp. II, P. Ital. V, P. Helv. V, P. Jap. IV, P.G. VI, P. Ned. V).** Prop. Name THIOCOL (Hoffmann-La Roche, London), available in powder, tablets and syrup.

$C_6H_3(OCH_3)(OH)SO_3K$  (1 : 2 : 3) = 242.2.

Dose.—8 to 15 grains (0.5 to 1 g.). thrice daily. Tablets contain 5 grains.

In colourless crystals with slight guaiacol odour, soluble in water, 1 in 6, slightly in alcohol. Contains 52% of guaiacol.

Has been recommended in phthisis, bronchitis and pneumonia, also for intestinal catarrh.

The commercial product is a mixture of two isomeric substances and consists of 3 parts of the compound with the  $(OCH_3)_2(OH)$  and  $(SO_3K)$  group in the positions 1 : 2 : 5 and 1 part of the 1 : 2 : 4 compound (using the notation adopted in the above formula). The 1 : 2 : 3 compound has never been prepared—A. H. Clark and E. Kirch, *J. Amer. pharm. Ass.*, 1935, 564.

**Morson's Soluble Creosote.**

Dose.—Up to 15 grains (1 g.) thrice daily

A light brown powder, consisting of the potassium salts of sulphonated fractions from beechwood creosote. It contains approx. 50% of total creosol and guaiacol oils and is soluble in water with slight flavour and agreeable after-taste. For bronchial affections.

**Créosol Dubois (Laboratoires Laleuf, Paris; Anglo-French Drug Co., London).** Monoguaiacolphosphate of calcium. 1 g. contains guaiacol 0.48 g., calcium

0.15 g., phosphoric acid 0.37 g. Supplied in the form of **Syrup Créosal** (1 dr. = 0.5 g. Créosal) for coughs and colds. *Dose*.—1 tablespoonful morning and evening, and proportionately smaller doses for children. Also as **[P1 81] Créosal (Dubois) for injection**.—A combination of sodium Créosal with sodium and strychnine methylarsenate. *Dose*.—1 ml. daily subcutaneously or intramuscularly in tuberculosis, lymphatic conditions, etc.

**Epidosin** (*Chemische Fabrik Güstrow, Güstrow s. Meckl.; Braun, London*), Methylene-diguaiacolacetylesther. Tablets contain 0.12 g. *Dose*.—10 tablets daily slowly dissolved in the mouth. For bronchial complaints.

**Guycose** (*Bayer Products, London*). Liquid "Somatose" (water-soluble meat albumoses) with 7% of calcium guaiacolsulphonate. *Dose*.—3 to 4 teaspoonfuls daily. In broncho-pulmonary affections, pneumonia, tuberculosis, etc.

**[P1 81 84] Kres-Lumin** (*Bayer Products, London*) Fluid preparation of calcium cresolsulphonate, containing Luminal  $\frac{1}{8}$  gr. to the teaspoonful. Expectorant and cough sedative.

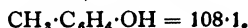
**Novocol-Calcium** (*Richter, London*) Calcium guaiacolphosphate in 4 gr. tablets or as a syrup. *Dose*.—1 or 2 tablets, or  $\frac{1}{2}$  oz. syrup, thrice daily. In catarrh of the upper respiratory tract, pharyngitis, bronchitis and tuberculosis.

**[P1] Pulmo** (*Bengué, London*) A solution of codeine phosphoguaiacolate, calcium phosphoguaiacolate, and sodium phosphoguaiacolate in organic combination. In subacute and chronic diseases of the respiratory organs.

**Resyl** (*Ciba, London*) Compound syrup containing glyceryl-guaiacol-ether. *Dose*.—3 to 5 teaspoonfuls daily. Expectorant and antiseptic in acute and chronic affections of the respiratory organs. Also in ampoules for intramuscular injection.

## CRESOL

*B.P., U.S.P. XI.*



*Syn.* ACIDUM CRESYLICUM, CRESOLUM CRUDUM (*P. Helv. V, P. Dan.*), CRESOLO GREZZO (*P. Ital. V*), CRESYL, PARACRESYLOL, CRESYL HYDRATE, METHYL PHENOL, METHYL HYDROXYBENZENE, KRESOLUM CRUDUM (*P. Hung.*).

**[P1]** "Phenols (any member of the series of phenols of which the first member is phenol, and of which the molecular composition varies from member to member by one atom of carbon and two atoms of hydrogen) except in substances containing less than 60%, weight in weight, of phenols, compounds of phenol with a metal, except in substances containing less than the equivalent of 60%, weight in weight, of phenols."

**[P2]** "Phenols as defined in Part I of this List (see [P1] above) in substances containing less than 60%, weight in weight, of phenols; compounds of phenol with a metal in substances containing less than the equivalent of 60%, weight in weight, of phenols."

**[83]** "Phenols—in Carvacrol; coal tar, crude or refined; creosote obtained from coal tar; essential oils in which phenols occur naturally; medicines containing less than 1% of phenols; nasal sprays, mouth-washes, pastilles, lozenges, capsules, pessaries, ointments, or suppositories containing less than 2.5% of phenols; smelling bottles; soaps for washing; solid substances containing less than 60% of phenols; tertiary butyl cresol; thymol."



[36] "*Phenols—specify proportion as the proportion of phenols (added together) contained in the preparation.*"

"*Compounds of phenol with a metal—specify proportion as the proportion of phenols (added together) that the preparation would be calculated to contain on the assumption that the compounds of phenols with a metal had been wholly converted into the corresponding phenols.*"

*Dose.*—1 to 3 minims (0.06 to 0.2 ml.). *U.S.P. XI* average dose 1 minim.

A yellowish brown liquid with tar-like odour. It is a mixture of ortho-, meta-, and paracresols, and forms the principal constituent in crude carbolic acids. **Ortho-cresol** (1 : 2) is a deliquescent solid, melting at about 30° and boiling at 191°. **Meta-** (1 : 3) is a colourless liquid, boiling at about 202°. **Para-** (1 : 4) melts at 36° and boils at about 201°. Sp. gr. 1.04 to 1.05.

*Fr. Cx* requires the following proportions: Ortho- 35, meta- 40, para- 25 *P. Helv. V*, *P.G. VI* and *P. Belg. IV* (*Cresol Brut*) require at least 50% *m-cresol* **Metacresolum** (*P. Helv. V*) contains at least 95%.

**Soluble** 1 in 50 of water almost completely. Miscible with alcohol 90%, chloroform, ether, castor oil and glycerin in all proportions. Also miscible with almond and olive oil in all proportions, but to make a clear solution about 1 in 2½ is necessary.

**Antidotes.** Treat as for poisoning by carbolic acid, *see* p. 745.

**Uses.** The mixed cresols are less potent in action than phenol (considered one-eighth as poisonous) and are used in many respects on analogous lines to the latter. Their odour is a disadvantage. Cresol is valuable for vaporising into the air in the treatment of whooping cough. It is largely employed in the manufacture of lysol (*Liquor Cresolis Saponatus B.P.*) and other disinfectants as described later. A small proportion (0.5%), preferably freshly distilled, is much used as an antiseptic to add to vaccines.

[P2] **Liquor Cresolis Saponatus (B.P.)** *Syn. and Prop. Names* **LYSOL** (this synonym may be used only in Gt. Britain and Northern Ireland, the name being a trade-mark in other parts of the world), **ACROSYL** (*Monsanto Chemicals, London*), **DIFFUSOL** (*Martindale, London*), **JEYSOL** (*Jeyes, London*), **KRESAPOL** (*Ferris, Bristol*), **LYCRYL** (*Eucryl, Southampton*), **MARSHALL'S LYSOL** (*Lysol, London*), etc.

Consists of 50% *v/v* of solution of cresol in a saponaceous solvent, any formula yielding a product complying with the *B.P.* characters and tests being officially recognised.

Many formulæ have been published—some employing linseed oil, as in the original lysol. Others proceed without heating, making the potash soap first by shaking, adding a proportion of alcohol and finally the cresol little by little. Others suggest an equivalent smaller proportion of soda instead of potash. The *B.P.* gives a method of preparation from saponified linseed oil, which is

satisfactory if the acid value of the oil is not less than 3 The *P G VI* method, which can be completed at room temperature, is also satisfactory, *vide infra*. In order to obtain a lysol miscible with water in all proportions, the cresol used should be free from xyenols, although the product then has a lower Rideal-Walker coefficient

[P2] **Liquor Cresolis Saponatus** (*U S P XI*)

A more uniform preparation than *B P* lysol, it contains 50% *v/v* of cresol and is made with prescribed quantities of linseed oil and potassium and sodium hydroxides

[P2] **Liquor Cresolis Saponatus** (*P G VI*), is made as follows —

Add a solution of caustic potash 27 in water 41, with shaking, to linseed oil 120, and then alcohol 12 Shake frequently at room temperature until saponified Finally, add cresol 200 and shake (All parts by weight) It may be necessary to allow to stand a day or so

These solutions are incompatible with acids

The Lysol Patent specification, 1017/1890 (expired) gives the following methods of preparation —

(i) Tar oil 100 g, linseed oil 100 g, caustic potash solution (1 in 2) 75 g, alcohol 65 g Boil with reflux condenser until saponified

(ii) Tar oil 40 g, common resin 10 g, caustic potash solution 70 g, alcohol 70 g

Points of value in cresols for making lysol — N Glass and A. J Jones, *Pharm J*, 11/1931, 76

There are several oils (corn, soya bean, coconut) just as desirable as linseed oil for compound solution of cresol Coconut oil makes a satisfactory product which shows a phenol coefficient from 50 to 100% higher than the coefficients shown by products made from other oils The price of coconut oil is slightly higher than linseed oil, but it apparently makes a product that is decidedly more efficient — P. L. Burrin, A. G. Worton and F. E. Bibbins, *J Amer pharm Ass*, 1935, 21, 1079

### **Antiseptics in Midwifery.**

The germicidal action of lysol in midwifery on streptococci, *e g*, *S. pyogenes*, is wholly inadequate in the dilutions which its caustic properties demand for clinical use No lysol can be other than a delusion. Lysol is only active on gram-negative bacteria. — L. P. Garrod, *Brit med. J.*, 1/1930, 413.

An investigation employing *Streptococcus pyogenes*. If prophylaxis can be served by merely bacteriostatic action, acriflavine is the most powerful agent. Adequate proportion would have to be maintained in the birth canal for several days. Few germicides possess adequate bactericidal action. Brilliant green is the surest safeguard against streptococcal infection (kills in 1 in 10,000 dilution) Next in order are Monsol, Izal and Cyllin. Acriflavine, Rivanol and one brand of lysol are on the border-line *Lysols when diluted to 1 in 400 have little margin of safe use*. Other lysols, mercurochrome and mercury salts found ineffective. — L. P. Garrod, *Brit. med. J.*, 1/1931, 572.

The Central Midwives Board and the L. C. C. drew attention to the variation in bactericidal power of lysol preparations and the strengths for use variously stated, but the Board, while giving the view that its use should be discontinued, gave no advice as to what should take its place.

Later the Central Midwives Board recommended (reissued from the L. C. C.) continued use of lysol provided it contains 50% of cresol — L. P. Garrod, *Brit. med. J.*, 1/1931, 572.

[P1] **Vapor Cresolis Compositus** (B.P.C.). Creosote 1, oil of eucalyptus 2, oil of Siberian fir 2, cresol to 100.

[P1] **Amyl-Meta-Cresol** (Boots, Nottingham). A powerful antiseptic of low toxicity, the outcome of research on the effect of alkyl groups in phenols. Occurs as a colourless solid, m.p.  $24^{\circ}$ , with pleasant odour and taste, sparingly soluble in water, insoluble in alcohol, ether and oils. Available as Amyl-meta-Cresol Antiseptic Solution for use as a mouth-wash or gargle, etc., 20 drops to a tumbler of tepid water, also in capsules containing 0.15 g. in olive oil. *Dose*—2 to 3 capsules thrice daily after meals, for use in chronic intestinal infection and colitis.

Phenol coefficient of from 200–300 against *B. typhosus*, *Streptococcus* and *Staphylococcus*—F. L. Pyman, *Lancet*, 1/1930, 759

**Cresineol** (British Drug Houses, London) A combination of cineole and cresol in 3 gr. tablets for use as an internal disinfectant

**Kerol Capsules** (Napp, London). Stated to contain an oxygenated diphenyl compound 60 times less toxic than phenol. Used as a gastric and intestinal antiseptic, the intestinal capsules being enteric coated.

[P1] **Trikresol** (Schering, London). A preparation of the three cresols, occurring as a colourless liquid slightly soluble in water. For surgical use  $\frac{1}{4}$  to 1% solution, as an eye wash 1 in 1000 to 1 in 2000.

[P1] **Trikresol-Formalin** in the proportion of 4 of Trikresol to 1 of solution of formaldehyde is a useful application as a dental dressing.

### Disinfectants.

The nomenclature used by manufacturers in describing their preparations includes the following:—

“**Tar Acids**” These are oxygenated hydrocarbons, including phenols, cresols and higher hydroxy compounds.

“**Phenoloids**.” A vague term. The bodies so called *simply consist of phenol and its higher homologues, i.e.,* xlenols and dimethylhydroxybenzenes. They are more bactericidal and less poisonous, and they make good emulsions with soap and water

“**Tar Oils**.” The neutral bodies present, *i.e.,* insoluble in soda.

“**Coke Oven Oils**.” Contain varying percentages of “phenoloids” with tar oils.

The disinfecting power of the higher phenols increases in proportion to their position in the homologous series, but their solubility *decreases* proportionately. Bodies, therefore, with the *hypothetical* diphenyl nucleus which have become so popular can only be used as *emulsions*

For various methods used for the determination of cresol and higher phenols in lysols and disinfectants, for meta-cresol in cresol, and for the Chick Martin and Rideal-Walker methods of standardising disinfectants, *see* Vol. II

### Proprietary Disinfectants

(For trade-names of various proprietary lysols, *see* under *Liquor Cresolis Saponatus* B.P., p. 428.)

[P2] **Creolin** (Pearson's Antiseptic Co., London). Contains 35% of the less toxic but more powerful homologues of phenol. R.W. coefficient 18–20. Used diluted 1–200 to 1–400.

[P2] **Creophen** (Ferris, Bristol). A coal tar product containing 25% *v/v* of phenols, with R.W. coefficient 5–6. Used as a general antiseptic in  $\frac{1}{4}$ –1% solution

[P2] **Cyllin Medical** (Jeyes Sanitary Compounds, London). A saponaceous solution of high boiling phenols with coal tar hydrocarbons in vegetable oil soap. It contains 50–55% *v/v* of phenols and has R.W. coefficient 22–24. For

medical and surgical purposes it is used diluted 1-300. For use in contact with mucous membrane, *e g*, douches, 1 in 600

[P2] **Cyllin Capsules**, containing 1 and 3 minims, keratin-coated, have been given as an internal antiseptic in summer diarrhoea, dysentery, colitis and sprue. "Stomachic" capsules, gelatin-coated, are also available.

**Lano-Cyllin Ointment** contains 5% of Cyllin in a wool fat and soft paraffin base. For eczema, ringworm, hæmorrhoids, etc.

[P2] **Izal** (*Newton, Chambers, Sheffield*) A coal tar product supplied as an emulsion containing not less than 40% of hydroxy carbocyclic compounds. For general use it is diluted 1-600 As a gargle 3-5 drops to a tumbler of warm water.

[P2] **Izal Capsules** contain 2 m, also 2 m with cod-liver oil 5 m. for use in phthisis

[P2] **Izal Medical** contains 40% *v/v* of phenols. Diluted 1-400 for septic wounds, ulcers, etc As an enema or gargle 10 to 13 m. in 5 to 6 oz of water Internally, it may be given in doses of 5 to 25 m in 1 oz of milk, lemonade or water

[P2] **Sanizal**. A cresylic disinfectant containing 24% of the homologues of phenol and giving an emulsion with water.

[P2] **Jeyes Fluid** (*Jeyes Sanitary Compounds, London*). A non-irritant and non-corrosive saponaceous solution of cresols and coal tar hydrocarbons with resin and vegetable oil soap. It contains 25-30% *v/v* of phenols and has R.W. coefficient 6-7

[P2] **Monsol** (*Monsol Ltd, London*). A non-caustic germicide stated to be prepared from oils obtained in the gasification of coal by the Mond power gas process. It contains 12% of the homologues of phenol, the formula being sulphonated cod-liver oil 17%, curd soap 3%, "Ol Picis (Mond)" 73%, terpinoline 2% and water 5%.

As a douche and for irrigations, etc, it is used diluted 1 in 500 to 1 in 250, for general use 1 in 20. Also available in the form of capsules, ointment, and throat pastilles The latter are stated to contain rectified oil of tar  $\frac{1}{4}$  m, oil of anise  $\frac{1}{2}$  m., oil of orange  $\frac{1}{2}$  m, in sugar basis (*For Neo-Monsol, vide p. 673.*)

[P2] **Pacolin** (*Pearson's Antiseptic Co, London*) Disinfectant containing 22% of the homologues of phenol. Is employed diluted 1-80 for general purposes, or 3-5 drops in a tumbler of water as a mouth-wash.

## CUPRUM

Cu = 63.57.

**Incompatibles with Copper Salts.** Alkalis and alkaline carbonates, also preparations containing tannin and iodides.

**Antidotes to Copper Salts.** Empty stomach by emetic (if vomiting has not occurred) or by stomach tube. Potassium ferrocyanide, 10 gr., in water is said to be a useful antidote. Keep patient lying down and warm; apply heat to abdomen. Give white of egg and demulcent drinks freely, but avoid oils and fats Morphine,  $\frac{1}{4}$  gr hypodermically, or tincture of opium by mouth, for pain.

**Cupri Acetas.**  $(\text{CH}_3\text{COO})_2\text{Cu} \cdot \text{H}_2\text{O} = 199.6$ .

*Dose.*— $\frac{1}{2}$  to  $\frac{1}{4}$  grain (0.005 to 0.03 g.).

Dark green crystals. Applied to ulcers acts as a stimulating caustic.

**Soluble** 1 in 15 approximately of water; only slightly in alcohol.

In tuberculosis has been given with sodium phosphate 1 gr., tragacanth mucilage  $\frac{1}{2}$  oz., or as *Pilula Cupri Acetatis*,  $\frac{1}{4}$  gr. in each with sodium phosphate 1 gr., powdered liquorice and glycerin *q.s.* The fatal dose *per os* is said to be 154 to 184 gr., and 154 to 308 gr. of the sulphate.

**Cupri Subacetas.** *Syn.* VERDIGRIS, AERUGO, COPPER OXY-ACETATE

Is usually of indefinite composition, approaching  $\text{Cu}(\text{C}_2\text{H}_3\text{O}_2)_2$ ,  $\text{Cu}(\text{OH})_2 \cdot 5\text{H}_2\text{O} = 369.3$  Occurs in blue needles or scales, efflorescing in air and becoming green Partly soluble in water with decomposition, insoluble in alcohol 90%, soluble in ammonium carbonate solution

**Linimentum Æruginis** (*Ph Lond*)

A decoction of verdigris, vinegar and honey, employed in veterinary work

**Cupri Chloridum.** *Syn.* CUPRIC CHLORIDE  $\text{CuCl}_2 \cdot 2\text{H}_2\text{O} = 170.5$

Dose —  $\frac{1}{4}$  to 2 grains (0.016 to 0.12 g)

Greenish very deliquescent crystals Use similar to that of copper sulphate

**Cupri Citras.**  $\text{C}_2\text{H}_3\text{O}_2\text{Cu} \cdot 2\frac{1}{2}\text{H}_2\text{O} = 360.2$

Greenish powder slightly soluble in water Used as an ointment for ulceration and granulation of the eye-lids

**LEPROSY** Copper citrate Dose —  $1\frac{1}{4}$  grains for an adult intravenously. It is readily made soluble in small bulk by 4 gr of sodium citrate — F J Palmer, *Brit med J*, 1/1925, 884, 11/1925, 96

**Unguentum Cupri Citratis** (*R.L O H*).

Copper citrate 20 gr, yellow soft paraffin to 1 oz

**Cuprentum** (*Allen & Hanburys, London*) 5% of soluble copper citrate in a lanolin base For ophthalmic use

**Cuprunc** (*Martindale, London*) is a copper citrate ointment supplied 5, 10, 15, 20 and 25% strength

**Cupri Nitras** (*B P C*) *Syn.* CUPRIC NITRATE  $\text{Cu}(\text{NO}_3)_2 \cdot 3\text{H}_2\text{O} = 241.6$

Deliquescent blue powder or crystals, very soluble in water and alcohol Used similarly to the sulphate in astringent lotions

**Cupri Oxidum.**  $\text{CuO} = 79.57$

Is supplied commercially as "precipitated" by adding caustic alkali to cupric sulphate solution, washing and drying, also "granulated" by heating to fuse partially.

**Cuprase** (*Ducatte, Paris, Anglo-French Drug Co, London*) Colloidal solution of copper hydroxide in 5 ml ampoules for very slow intramuscular injection for the treatment of cancer.

**Sterules of Colloidal Copper Solution** (*Martindale, London*) contain 5 ml of 1 in 2000 colloidal copper solution, to be rendered isotonic at the time of use For subcutaneous injection into inoperable malignant growths

**Cupri Sulphas** (*B P, U.S.P XI, P Helv V, P Dan.*)  $\text{CuSO}_4 \cdot 5\text{H}_2\text{O} = 249.7$

Dose. —  $\frac{1}{4}$  to 2 grains (0.016 to 0.12 g); as emetic, 5 to 10 grains (0.3 to 0.6 g). Average dose  $\frac{1}{4}$  to  $\frac{1}{2}$  grain (0.016 to 0.03 g.)

Blue crystals **Soluble** 1 in about 3 of water, 1 in 3 of glycerin, insoluble in alcohol 90%

**Uses.** Given internally in very small doses for severe diarrhoea and cholera, usually combined with opium (usually  $\frac{1}{2}$  grain of each), and has been tried as rectal injection also for internal hæmorrhage and intestinal ulcers Is a rapid emetic for narcotic poisoning, 3 or 4 grains in water every few minutes until vomiting occurs. Also suitable for acute phosphorus poisoning A solution of  $\frac{1}{4}$  to  $\frac{1}{2}\%$  is applied locally in eye affections (trachoma) as stimulant, and for gleet. For styes epilate the lashes affected and use 1 in 100 lotion 10 to 30 times a day The lashes grow again Copper points, in holders, are useful for eye and intra-uterine medication.

Membranous colitis in children has been treated by injection of solution of 4 gr. to 1 oz. with a little opium added

In dry skin affections, and in tubercular tendencies,  $\frac{1}{10}$  gr. doses thrice daily appear to act like arsenic, and are better tolerated

In pyorrhœa alveolaris the gums are "packed" with copper sulphate, and the patient directed to swab the gum with saturated solution of tannin in eau de Cologne; the tartar is frequently removed—Smale and Colver

Erosion in chronic endometritis has been treated by scarification and bathing with 7% copper sulphate solution

Actinomycosis and blastomycosis have been treated by internal administration and irrigation with 1% solution. In syphilis, treatment with copper sulphate and potassium iodide may prove useful

**ACTINOMYCOSIS** Treated by injection of 1% copper sulphate solution every few days until softening of the infiltration occurs. For small lesions a few ml. If extensive, the first injections are given under anæsthetic. Abscesses are opened and scraped and 40 to 100 ml of  $\frac{1}{4}$  to  $\frac{1}{2}$ % injected. Destruction of the fungus claimed—*Brit med J* *Expt*, 11/1922, 42

**AMOEBIC DYSENTERY.** Colonic irrigation recommended with 2 to 4 litres of hot solution of copper sulphate 1:5000 at a temperature of 50° to 55° in the container at the rate of 100 to 200 ml per minute. On arrival in the colon the temperature is 45° to 48°. Ten irrigations daily, or every other day, usually cured the condition—P. Beregoff, *Canad med Ass J*, 1/1935, 641

**CANCER OF THE UTERUS**—After curetting, copper sulphate 10% solution used as paint, and when the ulcer becomes callous a series of injections of colloidal copper. Then radium radiation—S. Forsdike, *Brit med J*, 11/1925, 839

**FISTULAS**, both tuberculous and osteomyelitic, well treated with injections of 2 to 3 ml of 10% solution—*J Amer med Ass*, 11/1926, 714

**TRACHOMA** well treated with subconjunctival injections of a 1% solution of copper sulphate with 4% procaine—*Per J Amer med Ass*, 11/1925, 1923

**Collyrium Cupri Sulphatis (B.P.C.)** 0.25% w/v

**Guttæ Cupri Sulphatis (R.L.O.H.)** 1 or 2 grains to the ounce. Suitable as a lotion for gleet

### ALIBOUR WATERS

**Aqua Cuprozincica Fortis** (*Fr. Ch. Supp.*, 1926) *Syn* EAU D'ALIBOUR FORTE. Copper sulphate 10 g, zinc sulphate 35 g, tincture of saffron 1 g, concentrated tincture of camphor (10% w/w) 10 g, distilled water to 1 litre

*It must be diluted for use with 5 or 6 times its volume of water, as a wet dressing in eczema.*

**Aqua Cuprozincica** (*Fr. Ch. Supp.*, 1926) *Syn* EAU D'ALIBOUR. Copper sulphate 1 g, zinc sulphate 4 g, tincture of saffron 1 g, concentrated tincture of camphor 10 g, distilled water to 1 litre

**Lotio d'Alibour (L.S.H.)** Copper sulphate 2, zinc sulphate 7, camphor water to 100.

**Lot. Cupro-Zincica (N.I.F.)** *Syn* ALIBOUR WATER

Zinc sulphate 12 gr, copper sulphate 8 gr, camphor water to 2 oz

**Lotio Zinci et Cupri Sulphatum (L.H.)**

Zinc sulphate 6 gr, copper sulphate 4 gr, camphor water to 1 oz

**Pasta d'Alibour (Strong) (L.S.H.)**

Zinc phenolsulphonate 1, copper sulphate 1, precipitated sulphur 5, diatomite 15, zinc oxide 30, lanolin to 100. The weak paste contains 0.1% of zinc phenolsulphonate, 0.5% of copper sulphate and 1% of precipitated sulphur

**Cuprum Aluminatum (P.G. VI, P. Helv. V)** *Syn* LAPIS DIVINUS.

Potash alum powdered 16 is mixed with powdered copper sulphate 16 and potassium nitrate 16, and melted with moderate heat in a porcelain dish. Camphor 1 and potash alum 1 are then added and the mass moulded or poured on to a plate to set.

*P. Jap* adds camphor 1 to 10 each of the other ingredients previously fused  
**"Brass Paste."** Formed by combining basic copper sulphate 86 with basic zinc sulphate 14.

TUBERCULOSIS, CUTANEOUS and other forms. Application to the conjunctiva of the everted eyelid resulted in the removal of all tuberculous tissue in a case of 20 years' duration.

A fluid preparation "brass oil" or "Bro" applied on gauze also used Further, picric brass paste containing 1% of picric acid found more penetrating — *H. A. Ellis, Lancet, 1/1919, 415.*

**Copper Alanine.**  $(CH_3CH(NH_2)COO)_2Cu = 239.8$  *Syn* COPPER AMINOPROPIONATE. *B. typhosus* and colon organisms are less resistant than *B. tuberculosis* to copper salts. As copper salts have a low toxic value in man, especially when given *per os*, inorganic salts of copper might be more widely used as bactericides. They exhibit a specially high toxicity toward protozoa.

Copper alanine is soluble in blood serum. It does not precipitate egg white, milk or solutions of caseinogen. 2 ml of 1 in 300 solution (commencing with 1 ml) has been given in inoperable cancer of the breast, without local or general inconvenience.

**Cu-Devenan.** A combination of copper and sodium thiosulphate, of value in syphilis. Spiricidal action considerable, with clearing up of rash and gummata, but effect on Wassermann reaction very slight. Well tolerated — *Brit. med. J. Epit., 1/1929, 102.*

**Cuprocyan** (*Instituto Naz. Medico Farmacologie Sersono, Rome*)

A double cyanide of copper and potassium, soluble in water and alcohol. Contains 22.26% of copper.

For the composition of *Benedict's and Fehling's Solutions*, and for an account of their uses for the determination of sugar in urine and other fluids, see Vol. II.

## DECOCTA

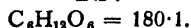
Decoctions of drugs are usually prepared 5% (unless otherwise stated) by boiling the drug in coarse powder with distilled water for 10 minutes and straining. If necessary a few drops of chloroform will preserve fresh decoctions for a reasonable period of time. For various decoctions consult index.

**Decocta Concentrata** are prepared commercially as a general rule "1 to 7." They should contain at least 20% of alcohol as a preservative. Fresh decoctions are preferable.

**Decocta (U.S.P. XI)** may be dispensed only if recently prepared

## DEXTROSUM

*B.P.*



*Syn. and Prop. Name.* MEDICINAL GLUCOSE (ANHYDROUS); GRAPE SUGAR; GLYCOSUM (*P. Helv. V*), SACCHARUM AMYLACEUM (*P. G. VI*), GLUCOSE OFFICINAL (*Fr. Cx. Supp., 1926*), DEXTROSOL (*Corn Products, London*).

A white crystalline or granular powder obtained by the hydrolysis of starch. It is an equilibrium mixture of  $\alpha$  and  $\beta$  dextrose. The B.P. requires not more than  $2\frac{1}{2}\%$  of moisture.

Dextrose monohydrate is also available, and is the form generally used for oral administration, being supplied under the name "medicinal glucose." It is the variety usually required when "glucose" *per se* is asked for. Dextrosium (U.S.P. XI) is the monohydrate.

Solid glucose, less pure, is in yellowish masses containing 10 to 20% of bodies allied to dextrin, *viz.*, amylin and gallisin.

**Soluble** 1 in less than 1 of water, 1 in 50 of cold alcohol 95%, 1 in 5 of boiling alcohol 90%; also soluble in glycerin.

**Uses.** Is given orally, intravenously or *per rectum* as a readily absorbed carbohydrate food in wasting diseases. It assists the metabolism of fats and prevents acidosis by raising the glycogen content of the liver. This action is utilised before the administration of drugs which may have a toxic action on the liver, such as cinchophen, neoarsphenamine, chloroform, etc. Before operations dextrose, in the form of barley sugar, may be taken *ad lib.* for the prevention of post-anæsthetic acidosis, and of delayed chloroform poisoning. Dextrose is also valuable for travel sickness, the vomiting of pregnancy and the cyclical vomiting of children. Hypertonic solutions (25%) are injected intravenously to relieve intracranial pressure by osmosis in meningitis and hydrocephalus, also to assist drainage of the accessory nasal sinuses. Isotonic dextrose is given intravenously in the treatment of shock.

Concentrated (50% or more) solutions have been used for the injection treatment of varicose veins. It is generally held that recanalisation and pulmonary embolism are more likely to occur with this than with other sclerosants.

#### **Oral Administration.**

**ACETONURIA** A heaped teaspoonful in half a teacup of cold water repeated every 2 hours for 4 or 5 doses, appears to give relief in practically all cases. 99% of cases of vomiting at sea are accompanied by increased acidity and acetonuria.—M. Fawkes, *Brit. med. J.*, 1/1925, 241

Persons suffering from sea-sickness, air-sickness, cyclic vomiting, car-sickness, migraine, asthma and acute gout, nearly always suffer from acetonuria and are relieved by massive doses of dextrose.—M. Fawkes, *Brit. med. J.*, 1/1929, 1133.

**ACUTE INFECTIONS AND CASES OF UNDER-NUTRITION**—Dextrose,  $\frac{1}{2}$  to 1 lb. daily with food of distinct benefit. (Normal persons can assimilate 200 to 500 g. in one dose without glycosuria).—T. Izod Bennett and E. C. Dodds, *Lancet*, 1/1929, 429. Cane sugar used similarly, good in typhoid and febrile diseases.—J. A. Ryle, *ibid.*, 515.

**ASTHMA IN CHILDREN**—Dextrose for prevention and treatment. Sugar as such, not as starch, prevented recurrence in four cases. Thought to be of no value in adults. Also of value in infantile eczema.—A. A. Osman, *Lancet*, 11/1929, 1187. (See, however, *ibid.*, 1283.)

**CARDIAC FAILURE**.—1 drachm doses of 5% solution *per os* apparently saved life.—G. Scott MacGregor, *Brit. med. J.*, 1/1921, 158; see also S. E. Denyer, *ibid.*, 248.

#### **Parenteral Administration.**

Barrington-Ward's *Abdominal Surgery of Children* advises a full diet and a bottle of barley sugar the day before the operation.



and more on the morning of the operation. When operation is severe and resistance low, 5% dextrose subcutaneously. Older children 10% per rectum.

**AS A SUMMARY** Always *before* a severe operation, (1) when liver efficiency is suspect, (2) when the metabolic rate is high, (3) when patient is under-nourished or emaciated always *after* a severe operation when blood transfusion is impossible *after* any anæsthetic (1) when loss of blood has been heavy and blood transfusion is impracticable, (2) in case of shock, (3) when it has not been given before the anæsthetic, (4) when a rough surgeon has operated, or more than the usual amount of anæsthetic has been used, (5) when there is a history of epilepsy.—F. P. de Caux, *Brit. med. J.*, 11/1929, 1005. (10% solution is preferred by this writer, given at 100°F.).

Intravenous injection has beneficial effect on the pulse and general strength, and in relief of thirst. By this means, water, the first need, is given in large amount with safety, and sugar to the extent of 2 ounces per diem without any demand upon the alimentary tract. Increased action of the kidneys is caused, and diluted toxic matters are removed.

The solution is also used intravenously with the addition at the time of use of 4 to 8 drops of adrenaline solution.

When a dehydrating effect is required hypertonic solutions are given intravenously or per rectum, as if given subcutaneously such solutions may cause œdema.

Intramuscularly a 10% solution in saline is relatively safe for raising blood sugar and when other methods contraindicated 20 to 40 ml. for infants, 100 ml. for older children or adults. The maximum rise in blood sugar occurs in  $\frac{1}{2}$  hour.—J. Glaser, *J. Amer. med. Ass.*, 11/1928, 726.

The adult body can utilise only 0.8 g. per kilo weight per hour. If given too rapidly it is promptly excreted through the kidneys and wasted.—*J. Amer. med. Ass.*, 11/1929, 1327.

Intravenously for adults, 75 g. in 300 ml. of water has been advised, given during 1½ hours.—*Lancet*, 11/1929, 723. Less, it is stated, will not give the maximum therapeutic effect, and more may produce over-stimulation of the insulin-producing activity of the pancreas. Single repeated doses preferable to prolonged injection. Half dose for a child and quarter dose for infant, but same length of time for injection.—P. Titus and H. D. Lightbody, per *J. Amer. med. Ass.*, 11/1929, 947.

**ARTHRITIS, CHRONIC.** A lowered dextrose tolerance is present in a large proportion of cases.—G. L. Kerr Pringle and S. Miller, *Lancet*, 1/1923, 171.

From 20 to 60, or even 100 ml. of 10% dextrose into the painful areas of the muscle and subcutaneous tissues gives immediate relief of pain in muscular rheumatism and lumbago. Also used with success in sciatica, etc.—*Brit. med. J. Epit.*, 11/1931, 8.

**BRIGHT'S DISEASE** with scanty urine. Contents of a Sterile diluted with a pint of distilled water intravenously—effect most satisfactory—Major G. W. Vincent, Maymyo, Burma, October 4, 1925.

**DIABETES, SEVERE**, treated, especially in cases where acidosis threatened—Sir W. H. Willcox, *Brit. med. J.*, 11/1921, 706.

Diabetic uræmia cured by intravenous injection of a pint of 25% dextrose solution in normal saline, repeated in 24 hours.—H. W. Fullerton and co-workers, *Lancet*, 1/1932, 559.

**JAUNDICE.** Intravenous injection of 500 ml. of a 10% dextrose solution may be indicated two or three times a day to rehabilitated patients with abnormally functioning livers. In jaundice, intravenous injections of 5 ml. of a 10% solution

of calcium chloride help to hasten coagulation of blood, prevent post-operative bleeding and neutralise the toxic bile pigments.—W Walters and W. J. Mayo, *J Amer med Ass*, 11/1925, 885.

**PNEUMONIA** The heart can be best helped by giving it food and oxygen. The best food is sugar. Intravenous injections of 10% dextrose are perhaps the most valuable when circulatory failing has commenced.—W. H. Wynn, *Lancet*, 11/1922, 496

**SEPTICÆMIA** Continuous giving of dextrose, up to 3 litres a day, drop by drop into the tissue of the breast, or into the saphenous vein, of great value in severe cases —Sir W. Wheeler, *Lancet*, 11/1931, 245

**TOXÆMIA** with gastric stasis well treated by intravenous injections of 10 g (1%) sodium chloride, and 100 g dextrose (10%), in 1000 ml. freshly distilled sterile water. Twenty minutes allowed for injection, 1, 2 or 3 litres being injected daily, supplemented by hypodermoclysis and proctoclysis —Per *J Amer med Ass*, 11/1925, 637.

**VARICOSE VEINS** A mixture of 50% dextrose and 30% sodium chloride thought to be the ideal solution. Dose—2 to 10 ml—not more than 20 ml at one sitting, with injections every other day —H. M. Kern and L. W. Angle, *J Amer med Ass*, 11/1929, 601

A 50% solution found the blandest and most efficient method of sclerosing. Inject 5 to 10 ml and then again 3 to 4 cm higher, repeat bi-weekly —G. de Takats, *J Amer med Ass*, 1/1929, 778

Up to 5 ml of 66% solution. There is a tendency for the clot to break up, and of the recorded instances of pulmonary embolism from varicose vein injections, the majority have occurred with dextrose —W. Levi, *Lancet*, 11/1930, 16

20,000 injections given without embolus. Massed statistics give 0.0024% mortality from that cause. Embolism probably in regions remote from the injection, as a result of inactive venous circulation. Ambulant treatment advised, wherever possible, but if rest in bed necessary, movement of limbs should be carried out frequently and patient encouraged to sit up —F. Remenovsky, per *Brit med J Epit.*, 1/1934, 27

**VOMITING OF PREGNANCY** Dextrose injections useful —V. J. Harding and B. P. Watson, *Lancet*, 11/1922, 649

Glucose intravenously 5 to 10%, 4000 ml in 24 hours —*Brit med J. Epit.*, 11/1930, 64

Intravenous injections of 50 to 75 g of dextrose in 200 to 300 ml distilled water (25% solution) used. The addition to the injection of 1 unit of insulin to 5 to 10 g of dextrose did not seem to have any clinical advantages. Vomiting usually ceased in 12 to 24 hours.—P. Titus, *J. Amer med Ass*, 11/1925, 491. W. Thalheimer gives 100 g of dextrose intravenously in as much water as the condition of the patient indicates (1 or 2 litres), the injection taking from 3 to 5 hours, and administers *hypodermically* 1 unit of insulin for every 3 g. of dextrose. Vomiting usually ceased in 6 to 8 hours —*Ibid*, 493

**Enema Dextrosi (B.P.C.).** Dose—4 ounces (120 ml) 10% w/v in water or peptonised milk

**Enema Dextrosi (St. M. H.).** Dextrose 1 oz, sodium chloride 1 dr, water to 1 pint

**Liquor Dextrosi et Sodii Chloridi (B.P.C.).** *Syn.* GLUCOSE-SALINE SOLUTION

A sterile solution containing 5% w/v of dextrose and 0.9% of sodium chloride. Although hypertonic when first injected, the rapid absorption of the dextrose renders the resulting solution isotonic.

**MODIFIED GLUCOSE SALINE SOLUTION.** Dextrose 250 g., acacia 50 g., magnesium sulphate 1 g., sodium bicarbonate 16.5 g., sodium chloride 30 g., potassium dihydrogen phosphate 0.9 g., potassium sulphate 1.75 g., water to 5000 ml. Dissolve the acacia in 50 ml. of water, strain, and autoclave at 110°. Allow to stand if possible for 24 hours. Filter through Gooch asbestos on a sintered glass filter, dissolve the dextrose and the salts except the

sodium bicarbonate, make up to 1000 ml., sterilise, allow to stand, filter, and again sterilise. Dissolve the sodium bicarbonate in 4000 ml. of water, add the saline solution, filter, distribute into flasks, displace the air by carbon dioxide, close the flasks with rubber bungs, tied down, and again autoclave. Has been administered in amounts of up to 20 pints in 4 days without causing rigor.—E. Lloyd, *Pharm. J.*, 1/1936, 399.

**Soluté de Glucose Hypertonique Injectable** (*Fr. Cx. Supp.*, 1926). Glucose 300 g., distilled water to 1000 ml.

**Soluté de Glucose Isotonique Injectable** (*Fr. Cx. Supp.*, 1926), is 5% isotonic solution, sterilised at 110° in neutral glass.

**Cabiven** (*Coates & Cooper, London*) A 66% solution of grape sugar for injection in varicose veins Issued in ampoules of 5 and 10 ml.

**Decrose** (*Boots, Nottingham*) Preparation of dextrose, calcium glycerophosphate and vitamin D. For use wherever dextrose is required, and especially in expectant and nursing mothers and growing children

**G.L. Glucose-D** (*Glaxo Laboratories, London*) 98% medicinal glucose with 4½ gr. of calcium glycerophosphate and 250 I.U. of vitamin D (calciferol) in each ounce. Especially indicated in conditions associated with ketosis in which glucose therapy is applied to patients who must subsist for long periods on a low fat diet.

**Glucose Sterules** (*Martindale, London*). Ampoules of dextrose solution containing sufficient to make 1 pint of 5% solution.

**Glucosum Liquidum** (*B.P.*). *Syn.* CORN SYRUP, GLUCOSUM (*U.S.P. XI*). Consists of a mixture of dextrose, maltose, dextrin and water, and occurs as a viscous mass containing about 20% of water *Sp. gr.* about 1.6 It is prepared by the hydrolysis of starch.

**Enema Glucosi Liquidi** (*B.P.C.*). *Dose.*—4 ounces (120 ml.). 10% *w/v* in water or peptonised milk.

**Pigmentum Glucosi** (*T.H.*) Glucose 25, glycerin to 100 For oæna.

**Syrupus Glucosi Liquidi** (*B.P.*). Liquid glucose 33.3% *w/w* with syrup. Used as a pill excipient.

**Dextrin** (*P. Helv. V*). *Syn.* BRITISH GUM. In yellowish powder or gum-like masses. Is obtained commercially by heating starch, which has been moistened with dilute nitric acid and dried, at 110° to 115°. Consists principally (there are various other dextrans formed before this) of achroodextrin which is the ultimate product of starch hydrolysis before the grape sugar stage is reached.

**Lactosum** (*B.P., P. Helv. V, P. Dan.*).  $C_{12}H_{22}O_{11}, H_2O = 360.2$ . *Syn.* SACCHARUM LACTIS, MILK SUGAR.

*Dose.*—*ad lib.*

Used in humanising cows' milk for infant feeding. Is diuretic and laxative in large doses. It is said to be a useful addition to magnesia as a laxative; it increases the solubility of the latter by combination.

A dose of ½ to 1 oz. in the morning in a large cup of weak tea a useful laxative. Of value in flatulence and spasm of the colon.—T. C. Hunt, *Lancet*, 11/1931, 872.

**Lævulosum** (*B.P.*). *Syn.* DIABETIN, FRUCTOSE.  
 $C_6H_{12}O_6 = 180.1$ .

A whitish, crystalline, hygroscopic powder, reducing Fehling's solution. It is laevorotatory.

A stronger sweetening agent than cane sugar; it has a pleasant flavour. Specially suitable for diabetics.

**Solubility.** Very soluble in water, less soluble in alcohol 90%; insoluble in dehydrated alcohol or ether.

**Lævulose Test for Liver Efficiency.** All ordinary sugars, dextrose, cane sugar, etc., when ingested, raise the concentration of sugar in the blood, but lævulose does not. Thus, with 50 g. of dextrose the blood sugar concentration is increased in the first half hour from the usual 0.1 to 0.16 or 0.17%, returning to normal in about 1½ hours. There is no rise with lævulose. This lack of power on the part of lævulose depends on an intact liver. If there is a definite lesion of the liver, lævulose acts, more or less, like dextrose, i.e., there is a marked increase in blood sugar.—J. C. Spence and P. C. Brett, *Lancet*, ii/1921, 1362; *Brit. med. J.*, ii/1922, 1061. See also Prof. Maclean, *ibid.*, 1060 and G. King, *Lancet*, i/1927, 388.

**Lævulose Tolerance Test** for hepatic efficiency in patients with epilepsy.—M. Gosden and J. Tylor Fox, *Lancet*, i/1929, 1351.

The most valuable and sensitive of all liver function tests and best shows early impairment. A healthy liver can dispose of 50 g. lævulose taken by the mouth without rise of blood sugar.—Sir Wm. Willcox, *Lancet*, ii/1931, 3.

**Sionon** (*Bayer Products, London*). *d*-Sorbitol,  $C_6H_8(OH)_6$ , a polyhydric alcohol closely related to the hexoses. A sweetening agent for use by diabetics. Does not reduce Fehling's solution nor yield an osazone.

Can safely be used as a substitute for sugar in diabetes, but the probability of intestinal irritation must limit the dose. Also its price makes it a luxury which can usually be more economically provided by the use of ordinary sugars and slightly more insulin.—W. W. Payne, R. D. Lawrence and R. A. McCance, *Lancet*, ii/1933, 1258.

Up to 30 to 80 g. daily may be given to diabetics with other foods.—*Per Prescriber*, 1929, 419. Can be metabolised more easily than glucose. Quantities up to 3 ounces a day rarely produce diarrhoea.—*Brit. med. J.*, ii/1930, 105.

**Manna** (*B.P.C.*, *U.S.P. XI*, *P. Helv. V*, *P. Dan.*).

*Dose*—½ to 4 drachms (2 to 16 g.), or more.

A saccharine exudation from *Fraxinus Ornus* (*Oleaceæ*). In flattish, somewhat three-edged pieces. Contains 40 to 60% of mannitol (*syn* mannite, *P. Ital. V*, *P. Ned. V*),  $C_6H_8(OH)_6 = 182.1$ , a non-fermentable sugar which does not reduce Fehling's solution and other sugars. Has mild laxative properties.

A report issued by an expedition of entomologists from the Hebrew University of Jerusalem states that manna is not an exudation from the tamarisk tree, but is an excretion from the bodies of the coccid insects, the amount varying with the abundance or scarcity of the winter rains. According to the late E. M. Holmes this does not prove that the tamarisk manna is the manna of Scripture, which occurs on plateaux in Central Africa, resembles coriander seed, is white in colour like hoar frost, sweet to taste, melts in the sun, and if kept overnight is full of worms in the morning.—*Chem. & Drugg.*, ii/1927, 429.

**Mel Depuratum** (*B.P.*). *Syn* CLARIFIED HONEY, MEL DES-PURATUM.

*Dose*—½ to 2 drachms (2 to 8 g.).

Prepared by melting honey, allowing to stand, straining off the scum rising to the surface and adjusting the sp. gr. to 1.36 by adding water.

**Oxymel** (*B.P.*). *Dose*.—½ to 2 drachms (2 to 8 ml.) Acetic acid 15, distilled water 15, purified honey to 100.

**Mel Boracis** (*B.P.*). *Syn*. BORAX HONEY, BORAX AND HONEY. Borax 10, glycerin 5, purified honey 85 (all by wt.).

**Sucrosium** (*B.P.*, *U.S.P. XI*, *P. Helv. V*, *P. Dan.*).  $C_{12}H_{22}O_{11} = 342.2$ . *Syn*. SACCHARUM PURIFICATUM, SACCHAROSE, SUCROSE.

In crystals or white powder.

In addition to the sugar obtained from the juice of the sugar cane, *Saccharum officinarum* (*Gramineæ*), various grades of granular cane and beet sugar, both with and without the addition of "blue," are marketed. For the manufacture of syrups a sugar

without the colouring matter is essential. *B.P.* and *U.S.P. XI* allow also beet sugar from *Beta vulgaris* var. *Rapa* (Chenopodiaceæ).

**Soluble** readily 2 in 1 of water, 1 in 60 of alcohol 90%

**Uses.** Is used for the same purposes as dextrose, but is not so readily assimilated since it has to be broken down in the body to dextrose before it can be stored as glycogen in the liver. It has been given intravenously as strong as a 50% solution, but an isotonic solution (920.6 grains per pint, i.e., 10.5%) would appear preferable. It is added to infants' foods made of dried milk.

Sugar with caraway infusion is used to hasten and increase mammary flow in Egypt, as well as to bring about a speedy involution of the uterus.

**RELATIVE SWEETNESS OF SUGARS.** If the sweetness of sucrose is rated as 100, lævulose deserves a value of 173, glucose 74, maltose 32, galactose 32, and lactose 16 — *J. Amer. med. Ass.* 11/1925, 977.

**Saccharum Ustum.** Caramel is prepared by heating sucrose at 180° to 200° to form a thick black mass which is diluted with hot water to a sp. gr. of 1.4.

**Liquor Sacchari Usti (B.P.C.)** is a mixture of equal volumes of burnt sugar and chloroform water.

### Syrupus (B.P.)

Sucrose 667, water to 1000 by weight. Sp. gr. not less than 1.32. 9 fl. oz. of syrup contain approx. 8 oz. of sucrose. *U.S.P. XI* orders sucrose 85, water *q.s.* to measure 100. Weaker strengths of syrup do not keep well. Potassium carbonate 1 grain in 12 ounces of syrup has been found to prevent crystallisation. Best temperature for producing syrup free from invert sugar is thought to be 90°.

**Invert Sugar** is prepared by action of dilute mineral acid on sucrose. It consists of a mixture of equal weights of dextrose and lævulose. A useful substitute for cane sugar in dyspepsia—more easily borne in gastritis.

Invert sugar forms in simple syrup on keeping—that made by cold process produces more than hot. In 18 months it may reach 6%.

### Invert Sugar Solution for Injection Treatment of Varicose Veins.

760 g. of sucrose is dissolved in water, 1 ml. of N/1 hydrochloric acid is added and the solution made up to a litre. After filtering, the solution is filled into 5.5 ml. ampoules which are sterilised at 120° for thirty minutes, inversion occurring simultaneously. This product has a pH of 3, but this is of no importance since the solution has no buffering action — Hansen, S. A. Schon and G. Tonnesen, *Dansk Tidsskr. Farm.*, 1933, 7, 26.

**Calorose (Braun, London)** Solution of invert sugar (either 40% or 74%) for subcutaneous and intravenous injection. A nutrient injection in place of glucose or glucose-saline.

**Theriaca, syn. TREACLE,** is the uncrystallisable residue from sugar-refining.

## DIGITALIS FOLIUM

*B.P., U.S.P. XI.*

*Syn. DIGITALIS, FOXGLOVE LEAF.*

[P1] "*Digitalis, glycosides of; other active principles of digitalis.*"

[81] "*Digitalis*, glycosides of, except substances containing less than one unit of activity (as defined in the 'British Pharmacopæia') in two grammes of the substance."

[86] "*Digitalis*, glycosides of, other active principles of *digitalis*—specify proportion as the number of units of activity as defined in the 'British Pharmacopæia' contained in a specified quantity of the preparation"

The leaf of *Digitalis purpurea* (Scrophulariaceæ) rapidly dried at a temperature of 55° to 60° as soon as possible after collection. *I.A.* requires the powdered entire second-year leaf, adopted by *Fr. Cx.* and *P. Belg. IV*; *P. Ned. V* specifies drying at 55° to 60°. *P. Helv. V* collects when dry, and dries immediately at 40° and then at 55° to 60° for  $\frac{1}{2}$  hour

**Incompatible** with preparations of cinchona and with lead acetate, also with iron salts (but the blackening is preventable by citric acid) and with iodine and potassium iodide.

**Cumulative Action.** The average rate of elimination is 25 m. of tincture, or about 2 gr. of standardised leaf per day, but it may be substantially more or less than this. Signs of toxic action are anorexia, nausea, headache and diarrhœa (nausea may be due to cardiac failure and not to digitalis), followed by runs of extrasystoles or ventricular tachycardia. Administration should be stopped for 24 hours, and smaller doses given afterwards.

The more common symptoms of overdosage, such as anorexia, nausea, vomiting, and diarrhœa are quite generally known. Less common phenomena justify re-emphasis. Coupled beats and the development of partial or complete heart block demand immediate discontinuation of the drug.

The toxic effects of digitalis on the brain and certain nerve tissues are not sufficiently appreciated although their importance is outstanding and they have been known to result in death. Prominent among these symptoms are disturbances in vision, consisting of dimness of vision, inability to focus the eyes, difficulty in the identification of objects, the presence of scotoma and diplopia, and yellow and green vision. The last are striking symptoms and are often alarming evidence of digitalis poisoning. Prodromal symptoms frequently occur and if properly interpreted, so that the administration of the drug is discontinued, the more prominent and serious disturbances may be avoided. They consist of restlessness, increased nervous irritability, and periods of disorientation regarding time and place. If stupor supervenes, death usually ensues. It is important to realise the fact that the cerebral manifestations of digitalis intoxication may occur independently of nausea, vomiting, and so forth. Occasionally, paroxysms of tachycardia occur, they usually arise in the ventricles, and have been known to result in death.—F. A. Willius, *Proc. Mayo Clin.*, 1935, 579.

**Antidotes.** Empty stomach by emetic or by stomach tube, using dilute tannic acid solution. Keep patient lying down and warm. Give stimulants, e.g., brandy,  $\frac{1}{2}$  oz., or aromatic spirit of ammonia,  $\frac{1}{2}$  dr., in water. Atropine,  $\frac{1}{100}$  gr., hypodermically. Chloral hydrate, 20 gr., may be necessary. Chloroform inhalations. Amyl nitrite has been recommended.

**Uses.** Digitalis is a valuable heart tonic and stimulant diuretic.

Digitalis has a narrowing influence upon the arteries. Acting on the vagus, it pulls the reins of the heart. Acting on the heart muscle, it is a most useful whip, at the same time providing it with food by improving the circulation. Slowing the heart, it makes it

regular also. This slowing gives the heart an opportunity of resting, so secondarily improving contractility, conductivity and excitability. By primary action it increases its strength, regulates its rhythm by depressing excitability and conductivity. In large doses it may increase excitability, causing extra-systoles, perhaps diminish contractility and by causing long pauses do harm to the circulation. All these influences vary according to dose, form in which it is given and the conditions of the heart. It may be tried with success in every case where the condition of the heart is the cause of a bad circulation or troublesome symptoms. In doubtful cases give small doses. It should be given a fair trial in every case. The only cases likely to show bad effects are those with damaged auriculo-ventricular bundle, in whom heart-block may result. Raised blood pressure is no contraindication to the use of digitalis, and is often due to some secondary effect of the heart failure.

When used as a diuretic the kidneys must be capable of responding to its action, which is exerted by increasing the force of the cardiac systole and forcing more blood through the organs.

**AURICULAR FLUTTER AND FIBRILLATION.** By pushing treatment a flutter can be converted into fibrillation, which may be replaced by normal rhythm on discontinuing the drug. Flutter may persist for years, but when ventricular rate is controlled by digitalis little additional burden appears to be placed on the heart.—J. C. Bramwell, *Lancet*, 1/1925, 1044.

Remarkable uniformity in reaction of cases of auricular fibrillation treated with digitalis—A. R. Gilchrist and D. M. Lyon, *J. Pharmacol.*, Aug., 1927, 319. 54 cases of auricular fibrillation treated with 0.1 ml. of tincture per lb weight, with sodium bicarbonate, aromatic spirit of ammonia, and chloroform water to 3 ounces. The average dose was 13 ml; the average pulse before use was 140 and 8 hours after it was 91. Toxic effects occurred once and vomiting twice, and the average duration of good effect was 6 days, so that small doses were needed at the end of a week. The method is a measure of urgency only.—G. J. Langley, *Brit. med. J.*, 1/1927, 1043, 1162.

**CARDIAC FAILURE.** Digitalis must be pushed to full legitimate limit. When it is consequent on fibrillation, digitalis gives its dramatic results. Strychnine, alcohol and camphor doubtful stimulants. There are very few specifics. A general account of the subject which will repay further study—J. Hay, *Brit. med. J.*, ii/1922, 899.

**CONGESTIVE HEART FAILURE.** Rest and digitalis the outstanding methods of treatment. *Digitalisation*—Calculate dose in minims by multiplying body-weight in pounds by  $2\frac{1}{2}$ , i.e., a 10-stone patient requires 350 minims. (Initially it is best to give  $\frac{1}{2}$  of this dose.) In urgent cases if no strophanthus or digitalis has been given previously, safest to give half the dose at once,  $\frac{1}{4}$  the dose after 6 hours,  $\frac{1}{4}$  after a further 6 hours, and a further  $\frac{1}{4}$  after 6 hours. Often not sufficient urgency to warrant more than 90 minim doses three or four times daily.—Maurice Campbell, *Practitioner*, 1931, 32.

**OVERWORK AND WEAKNESS.** Two minims of tincture thrice daily for a lengthy period with intermissions, as advised in Balfour's "Senile Heart."—"D.M.," *Med. Pr.*, Oct. 26, 1927.

**PNEUMONIA.** The infusion of digitalis helps the heart to resist depressant action which the pneumonia toxin has. 1 dr. of the infusion every 4 hours, increasing to  $\frac{1}{2}$  oz. every 4 hours, or 3 hours, night and day. Begin about second or third day.—E. M. Brockbank, *Brit. med. J.*, 1/1930, 974.

From a study of 1000 cases of lobar pneumonia no evidence was found that the routine use of digitalis was useful. When auricular fibrillation (in about 5% of cases) is present digitalis may save life, though patients frequently recover without it, but routine digitalis therapy in lobar pneumonia is dangerous.—H. Gold and co-workers, *Amer. J. med. Sci.*, April, 1933, 509.

**[P1-81] Acetum Digitalis (P. Ned. IV).** Digitalis leaves 1, dilute acetic acid (6%) 9, alcohol (90%) 1. Macerate 5 days.

[P1 81] **Digitalis Pulverata** (*B.P. Add.*).

*Dose.*— $\frac{1}{2}$  to  $1\frac{1}{2}$  grains (0.03 to 0.1 g.); single doses, 3 to 10 grains (0.2 to 0.6 g.).

Digitalis leaf reduced to powder, no part being rejected, and adjusted by admixture with exhausted leaf or with weaker leaf to contain 10 units per gramme.

For preparing the fresh infusion and the tincture, biologically standardised but unadjusted leaf is also recognised by the *B.P.*

[P1 81] **Digitalis Pulverata** (*U.S.P. XI.*).

*Average Dose.*— $1\frac{1}{2}$  gr. (0.1 g.).

Standardised dried and powdered leaf; 0.1 g. is equivalent to 1 to 1.1 *U.S.P.* digitalis units (which are identical with the international units).

[P1 81] **Tabellæ Digitalis Pulveratæ** (*B.P.C.*) contain 1 gr. (0.06 g.).

[P1 81] **Extractum Digitalis** (*Fr. Cx.*). Dried leaves extracted with 70% alcohol, evaporated to soft extract.

[P1] **Infusum Digitalis Recens** (*B.P.*).

*Dose.*—90 to 300 minims (6 to 20 ml.); single dose, 1 to 4 oz. (30 to 120 ml.).

Prepared from the equivalent of 0.5% of international standard digitalis powder. A concentrated infusion must not be used; when *Infusum Digitalis* is prescribed the fresh infusion is to be dispensed.

This is an active preparation. In use it may well be combined with some vasodilator.

*P. Ital. V* and *F.E. VIII* have 1% in boiling water. Length of infusion not defined. *P. Belg. IV* states prescribed quantities of leaves in water at 70°.

The infusion has such practical disadvantages that its use should now be abandoned—C Hoyle and J. W. Linnell, *Practitioner*, 1/1936, 94

[P1 81] **Liquor Digitalis ad usum internum** (*P. Ned. V*) *Syn.* DIGISOL.

*Dose.*—Maximum single 3 ml., maximum daily 10 ml

Similar to the solution for injection following except that, after the evaporation of the chloroform, the volume of water used to extract the residue is 88% of that of the chloroform. Finally to every 88 parts of this solution are added 12 parts of 96% alcohol

[P1 81] **Liquor Digitalis ad Injectionem** (*P. Ned. V*). *Syn.* DIGISOL FOR INJECTION. *Dose.*—5 ml. maximum single and *per diem*.

Macerate one part of powdered digitalis leaves with 8 parts of water during 48 hours at a temperature not exceeding 15°, strain and filter. Shake the filtrate with an equal volume of chloroform during 48 hours, avoiding emulsification. Reserve the chloroform solution and evaporate a measured volume of the aqueous layer on the water bath to a thick extract. To this add sufficient exsiccated sodium sulphate to form a dry powder. Shake this during 24 hours with a volume of the chloroformic extract equal to that of the evaporated aqueous solution and filter. Measure the volume of the chloroform and distil off. Treat the residue with water equal in volume to that of the chloroform, using small quantities at a time; dissolve 0.8% of sterile sodium chloride in the solution and filter. Sterilise by heating on 3 consecutive days for 1 hour at 70° to 80°. *Keep in a cool place away from light.*

A lethal dose for a cat of 2 ml. per kg. body weight is required by *P. Ned. V*. The preparation is considered to be too dilute for injection when rapid digitalisation is required.

[P1] **Mist. Digital. et Caffein. Cit.** (*N.I.F.*).

Caffeine citrate 2 gr., tincture of digitalis  $7\frac{1}{2}$  m., solution of strychnine hydrochloride 3 m., concentrated infusion of orange 15 m., water to  $\frac{1}{2}$  oz.



[P1] **Mist. Digital. c. Scill. (N.I.F.).**

Tincture of digitalis 5 m., tincture of squill 10 m., potassium acetate 10 gr., chloroform water to  $\frac{1}{2}$  oz

[P1 81] **Pilulæ Digitalis Compositæ (B.P.C.).**

Syn. GUY'S PILL, ADDISON'S PILL, BAILLIE'S PILL, PILULÆ DIGITALIS CUM SCILLA.

Dose.—1, as often as 3 times a day.

Mercurial pill 1, powdered digitalis 1, squill 1 In grains for one pill, in grammes for fifteen. Used in cardiac dropsy

[P1 81] **Pilula Hydrargyri et Digitalis Composita (St B. H.)**

Mercurial pill 1 gr, digitalis 1 gr, squill 1 gr, extract of hyoscyamus 2 gr.

[D P1 81] **Niemeyer's Pill. Syn HEIM'S PILL**

Dose.—1 pill thrice daily.

Powdered digitalis  $\frac{1}{2}$  gr., ipecacuanha  $\frac{1}{4}$  gr, powdered opium  $\frac{1}{4}$  gr., extract of helenium  $\frac{1}{2}$  gr

Used in combating the fever of phthisis. When the fever is of the periodical type, one grain of quinine sulphate is added to the above formula

The B.P.C. gives Niemeyer's Pill as a synonym for Pilulæ Digitalis Co. As pointed out by A. Fairlie (*Brit. med J*, 1/1935, 188) and confirmed by A Trimble (*ibid*, 288), Whittle gives the formula—digitalis  $\frac{1}{2}$  gr., quinine 1 gr, opium  $\frac{1}{4}$  gr, Heim's pill being similar with ipecacuanha  $\frac{1}{4}$  gr. in place of the quinine. In "Lectures on Phthisis" Niemeyer gives the formula of Heim's pill as above, with or without quinine, and says that "it has become a very common pill at my clinic."

[P1 81] **Tinctura Digitalis. (B.P., Fr. Cx, FE VIII, P Belg IV, and P. Ital. V)**

Dose.—5 to 15 minims (0.3 to 1 ml), single dose, 30 to 90 minims (2 to 6 ml.).

Frequently single doses of as much as 1½ drachms are given. Large single doses in many cases preferable to repeated small doses.

May be prepared from unstandardised leaf, the tincture being subsequently biologically assayed, or it may be prepared from standardised leaf, using a quantity equivalent to 1000 units (80 g of international standard powder) per litre, by percolation with alcohol 70%. The B.P. Add. permits also, as a further alternative, maceration for two days with alcohol 70% in place of percolation. It is required to contain 1 unit per ml

[P1 81] **Tinctura Digitalis (U.S.P. XI)**

Average dose —15 minims (1 ml).

Powdered digitalis leaf, 1 in 10, biologically standardised and adjusted so that 1 ml. is equivalent to 1 to 1 U.S.P. digitalis units.

**Stability of the Tincture.** Experiments extending over three years indicate that the addition of glacial acetic acid and sodium acetate to a tincture prepared from the de-fatted drug yields a stable preparation—L. W. Rowe and W. L. Scoville, *J. Amer. Pharm. Ass*, 1933, 1087.

In tropical climates such as that of India, tincture of digitalis undergoes deterioration in a short time Tinctures become darkish in colour on dilution

and are evidently considerably weaker in therapeutic efficacy. Dosage used in India far too small.—R N Chopra, S C Bose and P De, *Indian med Gaz*, Mar, 1925, 97

In cold countries the average quantity of tincture of digitalis required to cause toxic effects varies from 4 to 7 dr, but in Calcutta the smallest dose required was 9 dr and the highest 29 dr, while the average was well over 14 dr. Due to loss of potency of tincture and increased decomposition in the alimentary tract and liver. Toxic effects with B P tincture in 15 m doses thrice daily very rare in India. To obtain prompt results in grave cases 2 to 3 dr per dav for 5 days should be given.—S C Bose, *Indian med Gaz*, Apr, 1925, 154

[P1 81] **Digitalinum (B P C)** *Syn.* DIGITALINUM PURUM GERMANICUM. *Dose* (by subcutaneous injection)—For a single administration  $\frac{1}{2}$  to 1 grain (0.03 to 0.06 g), for repeated administration  $\frac{1}{15}$  to  $\frac{1}{4}$  grain (0.004 to 0.012 g.)

A mixture of glycosides from the seeds of *Digitalis purpurea* (Scrophulariaceæ) standardised biologically to contain 80 units of activity (equivalent to 8 g. of the international standard powder) per gramme. It occurs as an odourless, yellowish-white powder with an intensely bitter taste and contains digitalinum verum,  $C_{38}H_{56}O_{14}$ , a definite physiologically-active glycoside, together with a large proportion of water-soluble glycosides of which little is known and the physiologically-inactive glycosides digitonin,  $C_{55}H_{90}O_{29}$ , and gitonin,  $C_{49}H_{80}O_{28}$ .

**Soluble** readily in water and alcohol; sparingly soluble in chloroform and ether.

**Caution.** When digitalin is ordered (with the relative *bold dose*) Digitalinum (B P C) should be given. DIGITALINE CRYSTALLISÉE (*Fr Cx*) consists almost entirely of digitoxin, and the dose is much smaller, *v* Digitoxinum

[P1 81] **Injectio Digitalini (B.P C)**

*Dose* (by subcutaneous injection)—For a single administration, 15 to 30 minims (1 to 2 ml); for repeated administration, 3 to 6 minims (0.2 to 0.4 ml). Contains per ml 0.03 g of digitalin, equivalent to about  $2\frac{1}{2}$  units of activity

*Indications for hypodermic use*—

The hypodermic method alone is admissible (1) in grave cases where cardiac failure is imminent and immediate and certain action is required, because in such cases gastro-intestinal absorption is slow and uncertain (2) In cases in which it is desirable to safeguard the stomach and to avoid setting up gastric intolerance or embarrassment of cardiac action by a dilated stomach, the hypodermic method must be used, *e g*, in typhoid with failing heart, where diuresis is essential, in vomiting in arteriosclerotics, where the stomach becomes distended on the slightest irritation

[P1 81] **Nativelle's Crystallised Digitaline (Laboratory Nativelle, London)** is probably identical with digitoxin, *q.t.*;  $\frac{1}{10}$  mg. ( $\frac{1}{100}$  grain) contains one unit of activity. It is supplied in the following forms pink granules of  $\frac{1}{10}$  mg. ( $\frac{1}{100}$  gr.) and white granules of  $\frac{1}{2}$  mg. ( $\frac{1}{200}$  gr.), 1 in 1000 solution, 5 drops correspond to  $\frac{1}{10}$  mg. ( $\frac{1}{100}$  gr.), ampoules for intramuscular injection, 1 ml. =  $\frac{1}{2}$  mg. ( $\frac{1}{200}$  gr.), and ampoules for intravenous injection, 1 ml. =  $\frac{1}{2}$  mg. ( $\frac{1}{200}$  gr.) *Dose.*—(1) *small dose:*  $\frac{1}{10}$  mg. or 5 drops of the 1 in 1000 solution daily for the first 5 days of every 10 or 15-day period, continued indefinitely if necessary; (2) *medium dose* 2 granules of  $\frac{1}{2}$  mg. or 10 drops of the 1 in 1000 solution daily for 5 days, then cease for a week and repeat, or replace by the *small dose*; (3) *strong dose:* intensity of treatment depends upon the case, administration being pushed to saturation point as evinced by a pulse of 60; the patient should be examined daily and treatment stopped if signs of intoxication appear; the threshold is usually reached with 2 to 3 mg given over a period of 10 days

The intravenous or intramuscular injections are reserved for cases of intolerance to the medicament *per os*, or for cases of urgency.

[P1-81] **Tabellæ Digitalini et Nitroglycerini.**

Digitalin  $\gamma$  gr. (0.006 g.) with glyceryl trinitrate  $\gamma$  gr. (0.0006 g.).

Useful in aortic disease. Where vascular tension is high, the addition of glyceryl trinitrate prevents increase of peripheral resistance, and thus robs the digitalis of the influence on the arterioles on account of which its administration is supposed to be contraindicated.

[P1-81] **Digitoxinum (B.P.C.).** *Syn.* DIGITALINE CRYSTALLISÉE.

*Dose.*— $\pi$  to  $\pi$  grain (0.0001 to 0.001 g.). *Caution.*—0.002 g. may be a fatal dose.

Koppe took 1 mg. of digitoxin *per os* without any certain toxic effect, but a dose of 2 mg. taken four days later nearly produced a fatal result.—Prof. Cushny, *Brit. med. J.*, i/1925, 412.

Digitoxin of commerce consists chiefly of the definite glycoside digitoxin,  $C_{41}H_{64}O_{13}$ , together with a small proportion of gitoxin,  $C_{41}H_{64}O_{14}$ . *P. Belg. IV and F. E VIII* have formula  $C_{34}H_{54}O_{11}$ .

The content in the freshly harvested leaves is stated to be 0.25%.

It occurs as a white microcrystalline powder with an intensely bitter taste.

*Soluble* about 1 in 80 of dehydrated alcohol, also soluble in chloroform. Sparingly soluble in alcohol 90%; very soluble in more dilute alcohol. In the pure condition it is stated to be insoluble in water. There is, however, physiological and chemical evidence that it is *soluble in the presence of the other glycosides*.

Solutions may be made containing  $\pi$  gr. (0.001 g.) of digitoxin in 15 minims (1 ml.) of Petit's Liquor. This quantity will approximate 40 drops, which may be considered a maximum dose. Suitable either *per os* or as an enema. May also be given in syrup—digitoxin 0.1, alcohol (90%) 200, distilled water 750, syrup to 2500. *Dose*—1 to 4 drachms (4 to 15 ml.).

[P1-81] **Tablets** and [P1-81] **Granules** (Pills) of digitoxin are prepared containing  $\pi$  gr. ( $\frac{1}{2}$  milligramme) and  $\pi$  gr. ( $\frac{1}{10}$  milligramme).

[P1-81] **Digalen** (Hoffmann-La Roche, London)

Stable preparations of the therapeutically active principles of digitalis leaves, pharmacologically standardised, available as oral solution, tablets, ampoules and suppositories. 1 ml. of oral solution, and each suppository, is equivalent to 0.1 g. of international standard digitalis powder (1 B.P. unit), the tablets and ampoules are each equivalent to 0.05 g. of international standard powder ( $\frac{1}{2}$  B.P. unit).

The emergency intravenous dose of Digalen, for patients who have not previously received digitalis, is 1 minim per lb. weight, *i.e.*, one-half the full therapeutic dose. If necessary give another dose of  $\frac{1}{2}$  minim per lb. weight and repeat at 2-hourly intervals to a total of not more than 4 injections until improvement or signs of toxic action, then revert to oral use.—H. E. B. Pardee, *J. Amer. med. Ass.*, ii/1928, 147.

[P1-81] **Digifoline** (Ciba, London). Total glycosides of digitalis leaf. Tablets contain  $1\frac{1}{2}$  gr. (one tablet is stated to represent  $\gamma$  mg. of Digitaline Nativelle). *Dose.*—As a cardiac tonic, 1 tablet for 5 days in every fortnight, as a sedative, 3 tablets during 3 days, followed by interval of 10 days, asystolic dose, 4 tablets. Also given hypodermically or intravenously (1 ml. =  $1\frac{1}{2}$  gr. standardised digitalis leaf).

[P1-81] **Digifortis** (Parke, Davis, London). Tincture of digitalis free from fat. 1.25 unit per ml. *Average dose.*—8 minims (0.5 ml.) orally two or three times a day. Also Digifortis Tablets (0.8 unit) and Capsules (0.8 unit).

[P1-81] **Digitglusin** (*Lilly, London*). A standardised preparation containing all the medicinally active glycosides of digitalis. Supplied as tablets each representing 0.1 g. digitalis leaf or 1 cat unit, and as ampoules containing 1 ml. of the same potency.

[P1-81] **Diginutin** (*Burroughs Wellcome, London*). Preparations of the total glycosides of *Digitalis purpurea* in solution or tablets, for oral administration. The solution is equivalent in strength to the B.P. tincture, 1 ml. representing 0.1 g. of international standard digitalis. Tablets represent 5 or 10 minims of the solution.

[P1-81] **Digipuratum** (*Knoll, London; Pharmaceutical Products, London*). Active principles of digitalis. Dose—1 tablet, 1 ampoule, or 1 ml. of liquid (each corresponding to  $1\frac{1}{2}$  gr. of active digitalis leaves) 3 or 4 times daily.

[P1-81] **Digitalis Exclud Suppositories** (*Riddell, London*). Digitalis leaf 0.1 g., caffeine 0.09 g., theophylline 0.02 g. Dose—1 to 3 daily, for continuous treatment, one daily. Course of 20, then 14 days' interval and repeat. For use in the entire field of digitalis therapy, especially chronic heart complaints. No cumulative effects.

[P1-81] **Digitol** (*Sharpe & Dohme, London*). Defatted standardised tincture of digitalis.

[P1-81] **Verodigen** (*Boehringer, Mannheim; Pharmaceutical Products, London*). Gitalin component of digitalis leaves. Supplied in tablets or granules of 0.0008 g. and in suppositories containing 0.0012 g. Dose.— $\frac{1}{2}$  to 1 tablet, or 1 suppository.

[P1-81] **Digitalis Lanata** leaves, from the neighbourhood of the Danube, contain digitoxin, gitoxin, and digoxin,  $C_{41}H_{64}O_{14}$ , each glycoside existing in the leaf in combination with dextrose and an acetyl group forming respectively the complex glycosides, digilanid A, B, and C. Digilanid C is probably identical with lanadigin. The leaf of *D. lanata* is 3 to 4 times as potent as that of *D. purpurea*.

[P1-81] **Digoxinum** (*Burroughs Wellcome, London*).  $C_{41}H_{64}O_{14}$ . Dose.—Orally, initial dose 0.001 to 0.0015 g. ( $\frac{1}{80}$  to  $\frac{1}{40}$  grain), maintenance dose 0.00025 g. ( $\frac{1}{400}$  gr.) twice daily. To be taken with water. Intravenous dose, 0.0005 to 0.001 g. ( $\frac{1}{200}$  to  $\frac{1}{100}$  grain).

A crystalline glycoside obtained from *D. lanata*, m.p. (with decomposition) about  $265^{\circ}$ . Almost insoluble in water, sparingly soluble in chloroform and acetone, more soluble in dilute alcohol. Is rapidly effective when given orally in auricular fibrillation, but may be given intravenously when extremely rapid effect is required. Orally the effect begins in 1 hour, reaching a maximum in 6 to 7 hours; intravenously the effect begins in 5 to 10 minutes and reaches a maximum in 1 to 2 hours. Available in oral solution containing 0.0005 g. per ml., in tablets of 0.00025 g., or in solution for intravenous injection containing 0.0005 g. per ml.

5 to 10 minutes after intravenous injection of 0.75 to 1.0 mg. ventricular slowing begins and is maximal in 1 to 2 hours. 1.0 mg. intravenously causes a fall in rate slightly greater than that after intravenous injection of 0.25 mg. of ouabain of 90% standard activity. Digoxin by mouth in single doses of 1.0 to 1.5 mg. causes rapid fall in ventricular rate, beginning one hour after administration and reaching full extent in 6 to 7 hours. Digoxin is absorbed and eliminated more rapidly than digitalis and causes vomiting if sufficient is given. Congestion from congestive cardiac failure and auricular fibrillation diminishes after Digoxin. When oedema is present, diuresis occurs.—E. J. Wayne, *Clin Science*, per *Practitioner*, 11/1933, 314.

[P1-81] **Gitoxinum**.  $C_{41}H_{64}O_{14}$ .

A glycoside present in the leaves of *D. purpurea* and *D. lanata*, m.p. (with decomposition)  $285^{\circ}$ . Similar to digoxin in solubilities.

[P1-81] **Pandigal** (*Beiersdorf, Welwyn Garden City*). Preparation of the glycoside, lanadigin, from *Digitalis lanata*. Supplied in the form of tablets, solutions, ampoules or suppositories for oral, intravenous or rectal administration in doses of 0.0002 to 0.0004 g.

**Chemical Relationships of Digitalis Glycosides.** According to Prof. Stoll and co-workers, from the mixed glycosides of the leaf of *Digitalis lanata*, three complex glycosides named digilanid A, B and C respectively can be separated by shaking with immiscible solvents. Digilanid A on mild alkaline hydrolysis loses an acetyl group yielding deacetyldigilanid A. Similarly digilanids B and C yield deacetyldigilanids B and C. On further hydrolysis by means of an enzyme, a molecule of dextrose is removed from each of the deacetyldigilanids, and the products obtained are respectively digitoxin, gitoxin and Digoxin. The deacetyldigilanids A and B (but not C) can be separated from the mixed glycosides of *Digitalis purpurea* leaf, thus providing a connecting link between the therapeutically active principles of the leaves of the two species.

**Adonis vernalis** (*P. Austr., P. Ned. V*). Contains a hygroscopic glycoside adonidin which resembles digitalis in action. **Dose**—In powder, 3 to 6 grains, of infusion 1 in 40, 4 drachms, of adonidin,  $\frac{1}{4}$  to  $\frac{1}{2}$  grain daily. Epilepsy has been treated with it combined with bromide. **Tincture**—leaves and stalks employed, 1 in 10. **Dose**—10 to 30 minims. Adonidin is a local anæsthetic. In chronic glaucoma, iritis, and iridocyclitis 1% solution has been used, 3 drops relieve pain.

5 mg. of adonidin in 0.5% solution an efficient diuretic in cardiac anasarca.—*Per Yearb. Pharm.*, 1927, 218. See also *ibid.*, 1926, 237.

**Cereus** (*B.P.C.*), *syn.* NIGHT-BLOOMING CEREUS, CACTUS GRANDIFLORUS, is the fresh young shoots of *Cactus grandiflorus*. Preparations have been used as cardiac tonics free from cumulative or narcotic action, but evidence of utility is doubtful.

**Extractum Cerei Liquidum** (*B.P.C.*) *Syn.* EXTRACTUM CACTI GRANDIFLORI LIQUIDUM. **Dose**—1 to 10 minims (0.06 to 0.6 ml.) 1 in 1.

**Tinctura Cerei** (*B.P.C.*) *Syn.* TINCTURA CACTI GRANDIFLORI. **Dose**—2 to 30 minims (0.12 to 2 ml.) 1 in 4.

**Convallaria** (*B.P.C., P. Helv. V*) *Syn.* LILY OF THE VALLEY FLOWERS. The dried inflorescence of *C. majalis* (*Liliaceæ*). Two glycosides have been obtained from the plant. convallarin, a purgative (**dose**.—3 to 4 grains); and convallamarin (**dose**.— $\frac{1}{2}$  to 2 grains). A cardiac stimulant and diuretic. Its action is so feeble as to be almost of no value in medicine. It is an old remedy for dropsy.

**Extractum Convallariæ Liquidum** (*B.P.C.*) **Dose**.—5 to 10 minims (0.3 to 0.6 ml.) 1 in 1.

**Tinctura Convallariæ** (*B.P.C.*) **Dose**.—5 to 20 minims (0.3 to 1.2 ml.) 1 in 8.

**Cratægus Oxycantha** (*N.O. Rosaceæ*). *Syn.* ENGLISH HAWTHORN, HAW. **Dose**.—2 to 15 grains thrice daily. Liquid extract of the fruit, 10 to 15 minims. Contains a cyanogenetic glucoside. A cardiac tonic, in dyspnoea, hypertrophy, valvular insufficiency and heart oppression.

**Thevetin** (*Lilly, London*). A poisonous glycoside obtained from the seeds of *Thevetia nerifolia*, a tree indigenous to South America and the West Indies, India, the Hawaiian Islands and

**West Africa** Thevetin (empirical formula  $C_{29}H_{46}O_{13} \cdot 2H_2O$ ) is soluble in alcohol and water, and is relatively stable, a 1 in 20,000 aqueous solution retaining its physiological activity for more than a year.

**Dose**—For a typical case of heart failure—3 cat units (0.00275 g) in 2 ml intravenously 3 times a day till "digitalisation" is in evidence, then give a maintenance dose of 3 cat units every other day. It must not be given in full doses if the patient has been receiving digitalis or similar preparations.

In men with normal hearts, doses of 1 to 5 cat units of thevetin given by mouth reduced the pulse-rate by 9 to 20 beats per minute within 2 or 3 hours. Intramuscular injection had the same effect, but was painful. Trials on 23 patients with severe cardiac failure, using both the oral and the intravenous route, showed that the heart-rate was slowed, both in auricular fibrillation and when the rhythm was normal. Substituted for digitalis, thevetin gave the same results as that drug, the electrocardiogram usually showing changes similar to those produced by digitalis. Certain adverse effects on the gastro-intestinal system were noted—anorexia, nausea, vomiting, etc.—but these were more pronounced after oral administration of tincture of thevetia than after intravenous injection of thevetin. Disturbance of intracardiac conduction was observed in one case, while in another the patient died suddenly a few minutes after an intravenous injection, in this case the extent of previous digitalisation was uncertain. Biological assay has shown thevetin to have one-seventh of the toxicity and potency of strophanthin. The general conclusion is that thevetin, when given intravenously, has an action similar to that of digitalis, but more rapidly developed.—H. L. Arnold, W. S. Middleton and K. K. Chen, *Amer J med Sci*, Feb., 1935, 193.

**Xysmalobinum.** A bitter crystalline glucoside (0.3%) from the root of *Xysmalobium undulatum* (Asclepiadaceæ), a South African native remedy for dysentery and a bitter tonic. Toxic and has digitalis-like action.—J. M. Watt, *J Pharmacol*, Mar., 1930, 261. Isolation of glucoside.—*Trans Roy Soc S. A.*, 1927, XIV, 353.

Two glycosidal products have been separated from the root, which are similar in action to, and from 4 to 8 times as active as, xysmalobin. A pharmacological study.—J. M. Watt, *S Afr J med Sci*, 1935, 4.

## EMULSIONES

These are usually preparations containing oil and water in which the oil is finely dispersed in the water (oil-in-water type) or, *vice versa*, in which the water is dispersed in the oil (water-in-oil type).

The latter type is not usually employed for internal administration, but chiefly as liniments, embrocations and ointments, and the following considerations apply to the oil-in-water types only. Oil-in-water emulsions are very suitable preparations for exhibiting oily substances, particularly if they are nauseous, since, being suspended in an aqueous medium, which is generally sweetened and flavoured, they do not make contact with the papillæ of the tongue. Such preparations are, moreover, readily diluted with water and aqueous preparations. In order to make the dispersion of oil more permanent, it is necessary to employ an emulsifying agent or emulgent.

### Emulgents.

The following are used for preparing emulsions for internal administration—Acacia, decoction of chondrus (Irish moss), or yolk of egg.

**Acacia** is probably the best emulgent for this type of emulsion. When preparing an emulsion by hand, using a pestle and mortar,

it is better to employ powdered acacia, but if using a machine (hand or power) it is preferable to use mucilage of acacia. In the former method, a primary concentrated emulsion should first be prepared and afterwards diluted. The following proportions are suitable for making primary emulsions:—

For fixed oils: oil 4, water 2, gum 1

For volatile oils: oil 2, water 2, gum 1.

The powdered acacia should be added to the oil in the mortar, quickly diffused, the water immediately added and the emulsion prepared by light and quick trituration. In order to form an emulsion it is necessary that the acacia should hydrate with the water and this may not happen if the powdered acacia is left in contact with the oil too long before adding the water. The primary emulsion should be diluted to volume with the vehicle, any salts or alcoholic liquids being added in a diluted condition just before the final adjustment to volume.

Even a good emulsion may, on standing, tend to separate into two layers, an upper concentrated emulsion and a lower very weak emulsion. This is known as "creaming." An emulsion in this condition is readily made homogeneous again by shaking, but creaming will reoccur on standing. In order to prevent creaming, either the continuous aqueous phase must be made more viscous by the incorporation of more acacia or, better still, tragacanth, or the globules of the oily disperse phase must be decreased in size. In a hand mortar-made emulsion, using the proportions of oil and gum stated above, it is almost impossible to prevent creaming if the amount of oil present is less than 20%. By employing a machine, however, the oil globules can be reduced to such a very fine size that creaming can be prevented. Acacia emulsions usually require a preservative such as chloroform (0.2%) or benzoic acid (0.6%).

**Decoction of Chondrus.** This is a cheap emulgent and can be employed to replace acacia although it does not form such a good emulsion. It is preferable to use an emulsion machine as mortar-made emulsions are usually very coarse and are prone to separate. The decoction should be freshly prepared and allowed to stand for about 18 hours before use. If a machine is used, such as a small cream machine, equal volumes of the oil and decoction should be stirred together and the mixture passed through the machine twice. A preservative such as chloroform or benzoic acid is very necessary with this type of emulsion.

**Yolk of Egg.** This is an excellent emulgent for oils. It possesses approximately double the emulsifying power of powdered acacia, volume for weight. The yolk of an egg of average size measures from 4 to 5 fluid drachms and suffices for the emulsification of 4 fluid ounces of fixed oil or 2 fluid ounces of volatile oil. White of egg is a much poorer emulgent than the yolk and it is usual to reject it, using the latter only.

The yolk should be triturated to a perfectly smooth consistence and the oil gradually incorporated by trituration, water being added from time to time if the emulsion thickens too much.

Emulsions prepared with yolk of egg are not so liable to separate upon the addition of alcoholic preparations, acid salts, diluted acids, glycerin, syrups or large quantities of soluble salts as are those prepared with acacia. Preservatives are necessary for this type of emulsion.

Yolk of egg may be preserved by mixing it with an equal volume of glycerin, and by this means it can be kept in a suitable condition ready for use.

When preparing an emulsion in an homogenising or emulsion machine, it may happen that the resulting emulsion is too viscous, although when made by hand in a mortar the viscosity is a suitable one. The difference is due to the much smaller globules of oil in the machine-made emulsion, and it is advisable in this case to reduce the amount of emulgent specified in the formula.

*For details of hand machines for preparing emulsions, see Pharm J*, 11/1934, 307, 337.

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## ENEMATA

Enemas are aqueous or oily solutions or suspensions intended for rectal injection. They are given for their anthelmintic, nutritive, sedative or stimulating effects or for X-ray examination of the lower bowel. When they are intended to act merely in the rectum and to be retained, quantities up to 5 fluid ounces may be given, but for the large intestine and for lavage purposes, from one to two pints may be injected. All enemas should be given at body temperature.

The rate of absorption of substances when administered *per rectum* varies. Most of them are absorbed at approximately the same rate as when administered *per os*. Avertin has a high rate of absorption, dextrose, digitalis, paraldehyde, chloral hydrate, morphine salts and opium are quite readily absorbed, but considerable doubt exists as to the value of giving peptone or protein nutrient substances *per rectum*. The rate of absorption, according to some authorities, is so slow as to be of little value. The same is true of fats even when emulsified. It is usual to make enemas viscous in order to facilitate their retention in the rectum by using a mucilage of starch (2.5%) as a vehicle.

*For formulæ of enemata see under individual substances (vide Index).*

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## EPHEDRA

(with EPHEDRINE)

B.P.C.

Syn. MA-HUANG

[P1] "*Alkaloids, the following; their salts, simple or complex — Ephedra, alkaloids of*"

[83] "*Alkaloids—Ephedra, alkaloids of—in substances containing less than 1% of the alkaloids of ephedra*"

[86] "*Alkaloids—Ephedra, alkaloids of—specify proportion as the proportion of any one alkaloid of ephedra that the preparation would be calculated to contain on the assumption that all the alkaloids of ephedra in the preparation were that alkaloid*"

The dried young branches of *E. sinica* and *E. equisetina* from China, and of *E. Gerardiana* (Ephedraceæ) from India. It contains 1 to 2% of alkaloids of which 70% is *l*-ephedrine, other



alkaloids present being its stereoisomeride, *d*- $\psi$ -ephedrine, and small amounts of *l*-*N*-methylephedrine, *d*-*N*-methyl- $\psi$ -ephedrine and nor-*d*- $\psi$ -ephedrine. The *B.P.C.* requires not less than 1.25% of alkaloids.

Ephedra varieties and alkaloid content—*Pharm J*, 11/1927, 118

Indian varieties give good yield of pseudo-ephedrine, equally active and cheaper—R N Chopra, *Brit med. J*, 11/1931, 906

[P1] **Extractum Ephedræ Liquidum** (*B.P.C.*).

*Dose*.— $\frac{1}{4}$  to 1 drachm (1 to 4 ml) 1 in 1.

When dispensed in mixtures mucilage must be added.

**Phedros** (*Sharp & Dohme, London*) Each fl oz contains chloroform 2 m, liquid extract of ephedra 40 m, syrup of squill 180 m, syrup of ipecacuanha 40 m, ammonium chloride 8 gr, and syrup of tolu—*Dose* 2 teaspoonfuls every 2 or 3 hours

[P1] **Ephedrina** (*B.P.C., U.S.P. XI*)

$C_6H_5 \cdot CH(OH) \cdot CH(NH \cdot CH_3) \cdot CH_3 = 165$  1. *Syn.*  $\alpha$ -HYDROXY- $\beta$ -METHYLAMINOPROPYLBENZENE

*Dose*.— $\frac{1}{4}$  to  $1\frac{1}{2}$  grains (0.016 to 0.1 g)

An alkaloid obtained from various species of *Ephedra*. It occurs in white crystals which readily absorb moisture and carbon dioxide. As usually supplied it contains about 5% of water of crystallisation corresponding to the hemihydrate which has a m.p. of about 40°, the anhydrous crystals melt at about 38° (*B.P.C.* allows not lower than 35°.) The hydrated crystals can be dried by storage over calcium chloride.

**Soluble** 1 in 20 of water, 1 in 20 of glycerin, 1 in 100 of liquid paraffin (the solution being turbid unless made with anhydrous ephedrine), and in light petroleum, ether, alcohol and fixed and volatile oils. The solution in chloroform leaves a residue of ephedrine hydrochloride on evaporation.

**Dispensing Note.** Ephedrine preparations should be kept in stoppered amber bottles. Aqueous solutions undergo decomposition on exposure to light and air with formation of benzal-ephedrine. Oily solutions give very unpleasant-smelling compounds, probably amines, and eventually ephedrine carbonate and ammonia.

**Compatibility.** Both the sulphate and hydrochloride appear to be compatible in the cold with chemicals likely to be prescribed with them, e.g., the bromides, iodides, carbonates, bicarbonates, and sodium salicylate. Reasonable precautions are needed as ephedrine is a delicate alkaloid.

**Toxic effects** have sometimes been observed, consisting of giddiness, headache, thirst, nausea, palpitation, insomnia, and bladder irritation. Large and repeated doses should be avoided. Some patients need carefully regulated doses. Very large doses cause diaphoresis. For an adult a strong saline purge is suggested and a vasodilator if blood pressure is high, which is *not necessarily the case*.

Insomnia quite a characteristic effect with ephedrine. Sweating occurs with very large doses. No deaths have been recorded, but some quite serious collapse cases.—Prof Gunn, *Brit med. J*, 1/1929, 954

Chronic poisoning following  $\frac{1}{4}$  grain thrice daily for four months—W H. Higgins, *J Amer. med. Ass*, 1/1929, 313.

10 mg of ephedrine subcutaneously may cause gangrene and necrosis at the site of injection, but smaller doses do not. Adrenaline is said to be two and a half times as efficient as ephedrine.—J E Nadler, *Pharm J*, 11/1927, 73

**Uses.** Ephedrine is used in the treatment of asthma. It resembles adrenaline in its effects, but is effective when given orally. Its action is more prolonged, although not exerted for about 20 minutes after ingestion. It only controls minor degrees of bronchial spasm and is quite useless in severe paroxysms. Only solutions of the base or aqueous solutions of its salts are applied as a spray to the nose in hay fever and catarrh. It is also given internally in nocturnal incontinence, in myasthenia gravis and in narcolepsy, and has been suggested for use intravenously in obstetric shock and collapse and orally for the relief of nerve pains in leprosy. It is also sometimes used as drops or ointment for its mydriatic effect.

Many people fail to respond to ephedrine at all. There is frequently a transient fall in blood pressure initially, immediately followed by a well-marked rise, or rather, series of rises. The rise is much greater after injection than after oral use, but the latter has more lasting effect. Given by injection the rises rapidly succeed each other and are few, whereas orally the period between rises is longer and the series persists for an hour or more. The fall between rises is often precipitous, but does not go below the patient's normal blood pressure until the rises have ceased, when it falls considerably below normal and remains subnormal for about an hour. During the rises there is a feeling of well-being, but during the afterfall there is coldness, renal pain, hunger pain and sometimes colic.—J H Thompson, Discussion at the Roy Soc Med, *Brit med J*, 1/1929, 954

A warning concerning the misuse of vasoconstrictor drugs (adrenaline and ephedrine) as sprays, oils or drops for nasal troubles. Continuous and indiscriminate use may be fraught with disastrous results. On repeated use the duration of the constriction becomes gradually reduced, and in the end a condition of aggravated dilatation is produced.—A Francis, *Brit med J*, 1/1936, 609

**ASTHMA.** Though it has the advantage over adrenaline of effectiveness *per os* and giving longer immunity from attacks, it may cause tremor, palpitation, insomnia, and sometimes inability to micturate.—Frank Coke, *Brit med J*, 1/1929, 954. The first dose seems to act marvellously, but subsequent doses seem to do nothing.—J Freeman, *ibid*

Ephedrine *per os* for asthma found of value, but may cause subsequent difficulty in micturition.—M R Sagar, *Brit med J*, 11/1930, 716

A useful prophylactic agent. Psychological effect of being able to prevent acute attack. Peptide injections prior to ephedrine of value.—A Dingwall Fordyce, *Brit med J*, 1/1931, 166

The following injection hypodermically has been found useful in severe attacks.—Ephedrine hydrochloride  $\frac{1}{2}$  pt 1 liq Adrenalin 1 in 1000 5 m, pituitary extract 0.5 ml, distilled water to 1 ml. It should be put up in air-free ampoules, as otherwise it becomes discoloured.—M W Gefien, *Lancet*, 11/1932, 56

Failure of ephedrine to relieve some cases of asthma might be due to unusually small amount of adrenaline in circulation.—Rcp Pharmacol Lab, *Pharm Soc of Gt Britain*, 1932

Definitely better results when combined with thyroid medication.  $\frac{1}{2}$  gr dose of ephedrine hydrochloride twice daily gave little relief, but  $\frac{1}{2}$  gr dose at night with 1 gr of thyroid B.P. in the morning averted attacks for some months.—H S Russell, *Brit med J*, 1/1934, 1097

**ENURISIS IN CHILDREN.** Ephedrine  $\frac{1}{2}$  grain at bedtime for child from 10 to 12 almost specific. Bladder emptied before and 2 hours after going to sleep.—L E Parkhurst, *Brit med J*, 11/1930, 1103

The most useful drug at present available for treatment of enuresis in children. Give an initial dose of ephedrine hydrochloride at bedtime and increase by  $\frac{1}{2}$  gr every 4 to 7 days till enuresis is controlled, as much as 4 gr at a dose given

without unpleasant effects Wakefulness and restlessness respond well to phenobarbitone  $\frac{1}{2}$  gr. given with the ephedrine.—R. W Brookfield, *Brit. med J.*, 11/1935, 1119.

**HAY FEVER.** Treated with 1 gr doses *per os* in capsules, 5 to 10 capsules per week. Toleration varied. Worthy of trial in coryza—*Amer J. med Sci*, Oct., 1926, per *Pharm J*, 11/1927, 10

**LEPROSY.** *Per os* relieves nerve pains More lasting and efficient than adrenaline injections—E. Muir, *Indian med Gaz*, Apr., 1928, 198 See also R G. Cochrane, *Lancet*, 11/1929, 551, and R Green, *Trans R Soc trop Med.*, Jan., 1929, 376

**LOW BLOOD PRESSURE**  $\frac{1}{2}$  to  $\frac{1}{4}$  gr produces very satisfactory rise in pressure and no toxic symptoms.  $\frac{1}{2}$  gr caused giddiness.—H. W Hales, *Lancet*, 11/1928, 360.

**Chronic vascular hypotension.** Nine cases treated Rise in systolic pressure, remaining up for 4 hours—*Lancet*, 11/1928, 144.

Doses of 0.05 to 0.125 g *per os* or subcutaneously raise systolic and diastolic blood pressure, and increase pulse rate for several hours Also stimulate heart action and tend to increase output of urine.—T G Miller, per *J Amer med Ass.*, 11/1925, 1159

**Low blood pressure following influenza, pneumonia, etc** The power of ephedrine to raise blood pressure appears to be decreased in arteriosclerosis, debility and hypertension—*J Amer med Ass*, 1931, 96, 480

Warning against use in patients with cardiac injury—*Prescriber*, 1929, 70

**MYASTHENIA GRAVIS.** Personal experience of a medical victim after influenzal pneumonia. Progress with ephedrine after none with adrenaline and thyroid—H. Edgeworth, *J Amer. med. Ass*, 1/1930, 1136

Ephedrine in doses of  $\frac{1}{2}$  gr. twice daily of distinct value, the disease may, however, progress during its use. On theoretical grounds the action of ephedrine should be reinforced by an amino-acid such as glycine—D McAlpine, *Lancet*, 1/1934, 180.

**NARCOLEPSY** Symptoms successfully treated in eight cases by ephedrine hydrochloride or sulphate  $\frac{1}{2}$  gr 2 or 3 times daily—Henry Cohen, *Lancet* 11/1932, 335. See also A Haddow, *ibid*, 420

**OBSTETRIC SHOCK AND COLLAPSE.** 1 gr in 8 ml of normal saline intravenously Also in gynæcological cases to lessen shock of operation—J H Hannon, *Brit med J*, 1/1929, 954

**POST-OPERATIVE COLLAPSE** Ephedrine preferred to adrenaline—*Brit. med J. Epit.*, 1/1930, 16

**SHOCK FROM TRAUMA OR HÆMORRHAGE** Intravenous injection of 15 mg of value.—C. A. Johnson, *J Amer. med Ass* 1/1930, 1388

**SPINAL ANÆSTHESIA** Of value in restoring arterial tension. Give 0.1 g subcutaneously before systolic pressure drops below 100—*J Amer. med Ass*, 1927, 1136.

**STOKES-ADAMS' DISEASE.** 30 mg. of ephedrine sulphate by mouth gave instant relief from attacks and in one week the individual dose was cut down to 20 mg Medication ceased after a fortnight and there were no attacks for a year, when they were again relieved by ephedrine—C. S Higley and R M Stechen, per *Brit med J. Epit*, 1/1934, 27.

In six cases of complete heart-block ephedrine orally increased the rate of ventricular beating in four, and in two other cases complicated by Stokes-Adams' seizures, ephedrine taken for  $2\frac{1}{2}$  and  $1\frac{1}{2}$  years respectively was entirely successful in prevention of syncopal attacks, but seizures returned with its discontinuance The dose recommended is the minimum quantity consistent with an acceleration. A dose of  $\frac{1}{2}$  gr at 8-hour intervals may be sufficient—A. R Gilchrist, *Brit. med. J.*, 1/1934, 613

**WHOOPIING COUGH.** Dose of  $\frac{1}{2}$  grain *per os* in watery solution to children of one year and  $\frac{1}{2}$  grain for those younger, night and morning, of value Most useful during second stage No serious toxic symptoms—*Brit med J. Epit.*, 1/1928, 28.

# [P1] Nebula Adrenalinæ et Ephedrinæ Oleosa (B.P.C.).

Adrenaline 1 in 10,000 and ephedrine 1 in 50, with menthol and eucalyptol in an oily basis.

[P1] **Neb. Ephedrin.** (*N.I.F.*). Ephedrine  $4\frac{1}{2}$  gr., menthol  $2\frac{1}{2}$  gr., oleic acid 10 m., light liquid paraffin to 1 oz.

[P1] **Nebula Ephedrinæ Composita** (*B.P.C.*). Ephedrine 1% w/v with menthol, camphor and oil of thyme in light liquid paraffin.

[P1] **Unguentum Ephedrinæ** (*B.P.C.*). 1% in white soft paraffin.

[P1] **Ephetonin** (*Merck, Darmstadt; Martindale, London*) is ephedrine synthetically prepared. 4 mg. of the synthetic are stated to be equivalent to 2 mg. of the natural alkaloid

[P1] **Ephedrinæ Hydrochloridum** (*B.P., U.S.P XI, P. Helv. V, P. Dan.*).  $C_8H_9 \cdot CH(OH) \cdot CH(NH \cdot CH_3) \cdot CH_3, HCl = 201.6$ .

*Dose.*— $\frac{1}{4}$  to  $1\frac{1}{2}$  grains (0.016 to 0.1 g.). (*Caution:* 1 grain has been known to produce slight toxic phenomena. Many people react well to  $\frac{1}{10}$  grain.) *U.S.P XI* average dose  $\frac{3}{8}$  grain. *P. Dan* max single dose  $1\frac{1}{2}$  grains; max per day 6 grains. *P. Helv. V* gives  $\frac{1}{4}$  grain and 3 grains respectively. Colourless crystals.

*Soluble* 1 in 5 of water, 1 in about 5 of alcohol 90%, 1 in 60 of glycerin; insoluble in olive oil and in liquid paraffin.

### **Elixir Ephedrinæ Hydrochloridi** (*B P C*)

*Dose* —  $\frac{1}{2}$  to 2 drachms (2 to 8 ml)

A lemon-flavoured elixir containing  $\frac{1}{2}$  gr. of ephedrine hydrochloride per dr Asthma is well treated by 1 to 2 drachms at bedtime, also gives relief in hay fever. For whooping-cough in children  $\frac{1}{2}$  to 1 drachm.

[P1] **Nebula Adrenalinæ et Ephedrinæ** (*B.P.C.*).

Adrenaline 1 in 8000 and ephedrine hydrochloride 1 in 45 in an aqueous medium.

[P1] **Tabellæ Ephedrinæ Hydrochloridi** (*B P C*) contain  $\frac{1}{2}$  gr. (0.03 g.).

[P1] **Adrephine Inhalant** (*Parke, Davis, London*). Adrenaline 1 in 10,000, ephedrine hydrochloride 1%, benzocaine 1%, Chlorotone 0.5% and glycerin q.s. As a spray in hay fever, rhinitis, etc. [P1] **Adrephine Ointment** contains adrenaline 1 in 5000 and ephedrine hydrochloride 2%. For application to inflamed mucous membrane.

[P1] **Cosmo Brand Cough Syrup** (*Merck, Darmstadt, Martindale, London*) Contains Ephetonin 0.2%, Dionin 0.04%, and syrup of thyme.

[P1] **Ephetonogen** (*Richter, London*) Ephedrine hydrochloride 0.02 g., adrenaline 0.0001 g. *Dose.*—1 ml daily subcutaneously or intramuscularly.

[P1] **Ephregel** (*Evans, Sons, Lescher & Webb, Liverpool*) A combination of ephedrine and adrenaline as a nasal jelly for use in hay fever, rhinitis, and acute colds

[P1] **Ephrelux** (*Evans, Sons, Lescher & Webb, Liverpool*). Elixir containing per dr ephedrine hydrochloride  $\frac{1}{2}$  gr, codeine phosphate  $\frac{1}{2}$  gr, with squill and wild cherry *Dose* — 2 to 4 drachms

[P1] **Ephresol** (*Evans, Sons, Lescher & Webb, Liverpool*) Nasal spray containing ephedrine hydrochloride 2% and adrenaline 0.01%.

**Ephretuss** (*Evans, Sons, Lescher & Webb, Liverpool*) Syrup of ephedrine containing  $\frac{1}{2}$  gr of ephedrine per dr *Dose.*—Under 1 year, up to 1 drachm, over 1 year, up to 2 drachms; 2 or 3 times daily.

[P1] **Glucophedrin** (*Richter, London*) Suppositories for treatment of hæmorrhoids, containing glucose 1 g, ephedrine hydrochloride 0.05 g, Anæsthesin 0.03 g.

[P1] **Metaphedrin Inhalant No. 99** (*Abbott, Chicago; Pharmaceutical Products, London*) Contains ephedrine 1% and Metaphen (q t) 1 in 1500 Colds, asthma, hay fever, etc

[P1 81-84] **Nembutal and Ephedrine** (*Abbott, Montreal, Pharmaceutical Products, London*) Capsules containing Nembutal  $\frac{3}{4}$  gr and ephedrine hydrochloride  $\frac{1}{4}$  gr Asthma, hay fever, and other allergic conditions The addition of Nembutal has an antispasmodic and sedative effect

[P1 81] **Reflexor** (*Laboratoires de Sympathérapie, Neuilly-sur-Seine, Phargène, London*) Sympaphedrine (ephedrine) 0.154 gr, sympagerine (eserine salicylate) 0.000154 gr, aspirin 2.315 gr, phenacetin 0.77 gr, hyoscine hydrobromide 0.00031 gr, caffeine 0.386 gr Dose—1 dragée 2 hours after a meal, maximum dose 8 dragées per day Nervous disorders, asthma, hay fever, coughs, influenza, neuralgia and painful conditions

[P1 81 84] **Taumasthan** (*Haer, Basel, Chas Yarrow, London*) Tablets containing amidopyrine 0.1 g, theophylline 0.1 g, caffeine 0.05 g, ephedrine hydrochloride 0.01 g, agaric acid 0.0025 g, extract of belladonna 0.01 g Dose— $\frac{1}{2}$  to 1 tablet before retiring Asthma

**Zephrol** (*Pharmaceutical Specialties (May & Baker) Ltd, London*) Nasal jelly containing ephedrine hydrochloride, chlorbutol, sodium chloride and essential oils Zephrol spray solution and cough syrup, both containing ephedrine, are also supplied

[P1] **Ephedrinæ Sulphas** (B P C) ( $C_{10}H_{15}ON)_2 \cdot H_2SO_4 = 428.3$   
Dose.— $\frac{1}{4}$  to  $1\frac{1}{2}$  grains (0.016 to 0.1 g.) U.S.P. XI average dose  $\frac{3}{8}$  grain

White, colourless, odourless crystals, **soluble** 1 in 2 of water, 1 in 60 of alcohol 90%, 1 in 60 of glycerin, insoluble in oils

[P1] **Adrephine** (*Parke, Davis, London*) Adrenaline 0.01%, ephedrine sulphate 2% and Chloretone in solution Used as spray in hay fever, rhinitis, etc

[P1] **Epinalin** (*Burroughs Wellcome, London*) Each ml contains adrenaline 0.0001 g (= 1 in 10,000) and ephedrine sulphate 0.02 g (= 1 in 50) Nasal spray in asthma and hay fever Also supplied in ampoules for hypodermic injection

### [P1] **Pseudo-Ephedrine.**

Dose—Children  $\frac{1}{4}$  grain (0.015 g) for children under 7,  $\frac{1}{2}$  grain (0.03 g) for children over 7 Adults: 1 grain (0.06 g) repeated at hourly intervals until 3 grains has been given

Less toxic than ephedrine and much less effect on blood pressure Is more effective in lessening frequency of attacks in asthma of children, but not so effective in relieving an attack in adults Useful for prevention of dyspnoea in bronchitis and bronchial asthma

PRESSOR ACTION IN MAN was determined in 28 patients by subcutaneous injection 1 gr of pseudo-ephedrine caused a slight rise of blood pressure followed by a fall, while 2 gr produced a pronounced rise approximating to that obtained with 1 gr of ephedrine—S. B. Dimson, *Quart J Pharm*, 1/1934, 23 (Report to the Therapeutic Trials Committee)

Pseudo-ephedrine is of less value than ephedrine for controlling a fall in blood pressure during spinal anaesthesia—J. E. Monro, *ibid*, 32

PSEUDO-EPHEDRINE IN ASTHMA A report to the Therapeutic Trials Committee Per os it is more efficacious than ephedrine in lessening attacks of asthma in childhood, but less efficacious in relieving actual asthmatic paroxysm in adults Less toxic than ephedrine, but in large doses may produce the same unpleasant side-actions Worthy of further trial in children and in adults unable to tolerate ephedrine Neither ephedrine nor pseudo-ephedrine as effective as adrenaline injections in treatment of an asthmatic attack—G. W. Bray and L. J. Wits, *Lancet*, 1/1934, 790

Tests of ephedrine and pseudo-ephedrine at the Hospital for Sick Children, Gt Ormond Street, find both drugs wanting as a sure preventive of asthmatic

attacks, the best medicinal treatment for children being dilute hydrochloric acid before meals, with an anti-spasmodic at bedtime—Asthma Research Council Report, 1933, *Brit med J*, 11/1933, 1135

Useful for the minor manifestations of asthma but cannot replace ephedrine in the severe attacks—J B Christopherson and M Broadbent, *Brit med J*, 1/1934, 978

**Benzedrine** (*Smith, Kline & French, Philadelphia, Menley & James, London*) *Syn.* BENZYL METHYL CARBINAMINE, RACEMIC DESOXY-NOR EPHEDRINE, ISOMYN. A mixture of bases of the formula,  $C_6H_5CH_2CH(NH_2)CH_3$ , occurring as a colourless liquid volatilising readily at ordinary temperatures, and boiling at about  $202^\circ$ . On exposure to air it absorbs carbon dioxide, forming a carbonate which is also readily volatile. It resembles ephedrine and adrenaline in properties, and is used as a volatile vasoconstrictor in hay fever and for the relief of acute coryza and all catarrhal affections of the respiratory system. It is available in the form of an inhaler packed with Benzedrine 0.325 g., oil of lavender and menthol. Internally it is stimulant to the central nervous system, raises blood pressure and relaxes smooth muscle. It has been administered as Benzedrine sulphate in tablets containing 10 mg. in the treatment of narcolepsy, pyloric spasm and post-encephalitic parkinsonism.

**HYPOTENSION.** An investigation of blood pressure in mental disorders. Benzedrine sulphate given orally causes a rise in blood pressure, commencing in 45 to 120 minutes, reaching a maximum in a further 60 minutes and returning to normal in 24 hours. All patients showed increased talkativeness and frequently there was a tendency in the direction of euphoria—S A Peoples and E Guttmann, *Lancet*, 1/1936, 1107.

**NARCOLEPSY.** Complete relief of attacks of sleep and almost complete relief of catalepsy obtained in nine cases from use of Benzedrine 10 to 40 mg. 3 times a day. Start with 10 mg. doses to avoid untoward symptoms. Approximately three times as effective as ephedrine in preventing attacks of sleep—M Prinzmetal and W. Bloomberg, *J Amer med Ass*, 11/1935, 205.

**Par-Isalon** (*Wiernik, Berlin, Coates & Cooper, London*) Tablets containing Isalon (1-phenyl-2-[methyl(diethylaminoethyl)]-aminopropane-1-ol—*Gehe*), theobromine, caffeine and phenazone. For bronchial asthma, chronic bronchitis, angina pectoris, etc.

**Isalon** is an ephedrine substitute stated not to have the blood-pressure-raising effect of ephedrine, but to have a good action on the bronchial muscles. Of 60 cases treated (0.09 g. in tablets thrice daily during attacks and half this dose during quiescent periods) 22 were cured and 28 much relieved, with no observable effect on blood pressure or pulse rate and no toxic symptoms—H Handovsky and E Kubeja, *Munch med Wschr*, 1934, 326.

**Euphorbia** (*B.P.C.*) *Syn.* AUSTRALIAN SNAKE WEED, CAT'S HAIR, EUPHORBIA PILULIFERA. The dried entire plant, *E. hirta* (Euphorbiaceæ).

For asthma, bronchial affections, paroxysmal dyspnoea, laryngeal spasm, whooping cough, angina pectoris, in coryza and hay fever.

**Euphorbia Extract** (Aqueous) *Dose*  $-\frac{1}{2}$  to  $1\frac{1}{2}$  grains.

**Tincture.** *Dose.*—10 to 30 minims 1 in 5 of alcohol 60%.

**Extractum Euphorbiæ Liquidum** (*B.P.C.*).

*Dose*—2 to 5 minims (0.12 to 0.3 ml.) 1 in 1.

[P1] **Mist. Euphorb. Co.** (*N.I.F.*) Potassium iodide  $7\frac{1}{2}$  gr., sodium bromide  $7\frac{1}{2}$  gr., liquid extract of euphorbia 10 m., solution of glyceryl trinitrate 1 m., ethereal tincture of lobelia  $7\frac{1}{2}$  m., water to  $\frac{1}{2}$  oz.

**Euphorbia Peplus** (Euphorbiaceæ). *Syn.* PETTY SPURGE, DEVIL'S MILK  
The entire plant. Indigenous to the British Isles

In cases of dyspnoea, whether of pulmonary or pneumogastric origin. Modifies secretion in asthma and suppresses attacks. The fresh plant has an acrid juice which, when dried, imparts its virtues both to water and alcohol. Decoction—45 grains to the pint. *Dose*—1 teacupful (diluted if preferred) 3 or 4 times daily, preferably between meals. **Extract.** *Dose*—7½ to 30 grains. **Tincture** (1 in 5 with 45% alcohol). *Dose*.—30 to 60 minims during the day.

**Costus.** *Syn.* KUNTH, KUTH OR KOOT ROOT. The root of *Saussurea Lappa* (Compositæ). In powder it is used for preserving furs, etc., from moth. The oil is used as a basis for perfumes the powder for sachets.

A **Liquid Extract** 1 = 1 made by percolation with 90% alcohol to exhaustion and concentrating. Used for the treatment of asthma. ½ to 2 drachms stated to stop paroxysms. It may be taken as such in a little water (to cut short a paroxysm), or in the form of a mixture, taken 3 to 4 times daily, containing potassium iodide or potassium bromide 5 to 10 gr, tincture of belladonna 3 to 5 m, borax 2 gr, liquid extract of *S. lappa* ½ to 2 dr, spirit of chloroform 10 m, water 1 oz., for continued administration. Has no cumulative action. Is not claimed to produce a permanent cure—R. N. Chopra, *Indian med. Gaz.*, Apr, 1928, 189, *Indian J med Res.*, 1929, 351.

## ERGOTA

### B.P.

*Syn.* SECALE CORNUTUM (U.S.P. XI, P. Ital V, P. Helv V, P. Dan., P. Belg. IV), ESPOLÓN DE CENTENO, CORNEZUELO DE CENTENO (F.E. VIII).

[P1] "*Alkaloids, the following; their salts, simple or complex—Ergot, alkaloids of.*"

"*Ergot (the sclerotia of any species of Claviceps); extracts of ergot; tinctures of ergot.*"

[81] "*Alkaloids, the following; their salts, simple or complex:—Ergot, alkaloids of.*"

"*Ergot; extracts of ergot, tinctures of ergot.*"

[86] "*Alkaloids—Ergot, alkaloids of—specify proportion as the proportion of any one alkaloid of ergot that the preparation would be calculated to contain on the assumption that all the alkaloids of ergot in the preparation were that alkaloid.*"

*Dose.*—The B.P. requires Ergota Præparata (*vide infra*) to be dispensed when Ergota is prescribed. Fr Cx, maximum single dose 15 grains; maximum during 24 hours 60 grains approximately.

The sclerotium of the fungus *Claviceps purpurea* (Pyrenomyces) on *Secale cereale* (Gramineæ). It contains not less than 0.05% of ergot alkaloids calculated as ergotoxine. The B.P. assay is colorimetric and determines total alkaloids; that of the U.S.P. XI is biological (cock's comb method—see Vol. II).

**Storage.** Ergot should be kept entire and not powdered. If powdered the fat should be removed immediately, otherwise the alkaloid content decreases.

**Antidotes.** Empty stomach by emetic or by stomach tube, using dilute solution of tannic acid. Keep patient lying down and warm. Give purgative dose of castor oil or magnesium sulphate.

Medicinal charcoal has been recommended. Stimulants, *e.g.*, brandy,  $\frac{1}{2}$  oz., or aromatic spirit of ammonia,  $\frac{1}{2}$  dr., in water Nitroglycerin sometimes used.

**Uses.** Almost entirely for its action on the uterus, stimulating muscular contraction, and so checking hæmorrhage after parturition and from the presence of fibroid tumour, also to promote involution. It is also used as an emmenagogue.

Ergot causes spasms of arterioles and rise of blood pressure by acting directly on the vessels, independently of the central nervous system. It must not be used, therefore, in the treatment of cerebral hæmorrhage although it is considered useful by some clinicians in pulmonary hæmorrhage. It is useful in polyuria and chorea, and is also given to check night sweats, spermatorrhœa and menorrhagia.

All diseases in which a drug inducing muscular contraction is indicated should, according to some authorities, be treated by ergot, *e.g.*, disturbances of the circulatory system, skin affections, acne rosacea, pruritus, also nervous complaints (*e.g.*, excessive smoking).

For disordered circulation, migraine (hypodermically), alcoholism, hysteria and in acute inflammatory infections—meningitis, pneumonia, pericarditis—ergot has also been used.

For hæmoptysis and pneumonia it is of little utility—*Brit. med. J.*, 1/1930, 1007.

**ENURESIS IN CHILDREN** Ext. Ergot. Liq 5 minims for a child of 5 years, with 2½ minims Ext Glyc Liq and a drop of peppermint effectual in a fortnight. Worth trying.—A. Patton, *Brit. med. J.*, 11/1930, 981.

[P1 81] **Ergota Præparata (B P)**

**Dose.**—5 to 15 g. (0.3 to 1 g.); it may be given in a cachet or capsule.

Powdered and defatted ergot adjusted to contain 0.1% of ergot alkaloids calculated as ergotoxine. Probably the best ergot preparation for giving *per os*.

*P Helv. V* requires the defatted powder to be used in dispensing and for preparing galenicals (unless the contrary is specified), the dose being reduced by 30%.

[P1 81] **Erbolin (Glaxo Laboratories, London)** A stable physiologically standardised preparation of powdered, defatted ergot in capsules, each containing the equivalent of 0.5 mg. ( $\frac{1}{200}$  grain) of ergotoxine.

[P1 81] **Extractum Ergotæ (B.P.C.).**

**Dose.**—1 to 3 grains (0.06 to 0.2 g.).

A soft extract containing when freshly prepared 0.5% of alkaloids; 3 gr. contain about  $\frac{3}{80}$  gr. of total alkaloids. The extract is much more stable than the liquid extract, its alkaloidal content being practically unaltered after two years' storage under ordinary conditions.

[P1-81] **Extractum Secalis Cornuti (P. Ital. V, F.E. VIII, P. Belg. IV, Fr. Cx.).** *Syn.* ERGOTINA BONJEAN, ERGOTIN.

**Dose.**—2 to 8 grains (0.12 to 0.5 g.).

An aqueous extractive precipitated by alcohol and evaporated.



**[P1 81] Extractum Ergotæ Liquidum (B P).**

*Dose* —10 to 20 minims (0.6 to 1.2 ml).

Prepared from defatted ergot by percolation with a 1% solution of tartaric acid in alcohol 50%, and adjusted to contain not less than 0.06% *w/v* of total ergot alkaloids, calculated as ergotoxine, when freshly prepared. It loses activity on keeping, and the *B P* permits a decrease in alkaloidal content to 0.04%.

*Fr Cx*, 1 = 1 by weight. Maximum dose during 24 hours 6 g. Prepared by macerating with water containing 0.05% of tartaric acid, and further treatment.

**[P1 81] Fluidextractum Ergotæ (U S P XI) Average dose** —30 minims (2 ml)

The potency per millilitre is equivalent to not less than 0.5 mg of ergotoxine ethanesulphonate. It is prepared by extracting defatted ergot with a menstruum consisting of 2 volumes of hydrochloric acid and 98 volumes of diluted alcohol (48.4 to 49.5% *v/v*) or by extracting ergot with the same menstruum and, after cooling to -14°, removing the congealed fat by filtration. One ml represents 1 g of ergot, the liquid extract must not be diluted and it must conform in potency to the above standard when assayed biologically, using single comb White Leghorn cockerels.

**[P1 81] Ergodex (British Drug Houses, London)** *Dose* —10 to 30 minims (0.6 to 2 ml). A stable liquid preparation containing the whole alkaloidal content of ergot, including the alkaloid ergometrine, and suitable for oral use.

**[P1 81] Infusum Ergotæ Recens (B P C)**

*Dose* —1 to 2 ounces (30 to 60 ml) 1 in 20

The fresh infusion should be dispensed when Infusum Ergotæ is ordered.

**[P1 81] Mistura Ergotæ Alkalina (St M H)** Liquid extract of ergot 20 m, iron and ammonium citrate 15 gr, weak tincture of ginger 20 m, chloroform water to 1 oz.

**[P1 81] Mistura Bromidi cum Ergotæ (C H W)** Potassium bromide 10 gr, liquid extract of ergot 5 m, cinnamon water to 1 oz.

**[P1 81] Mistura Ergotæ cum Ferro (C H W)** Liquid extract of ergot 15 m, solution of ferric chloride 10 m, spirit of chloroform 10 m, infusion of columba to 1 oz.

**[P1 81] Mistura Ergotæ cum Strychnina (R F H)** Liquid extract of ergot 30 m, quinine sulphate 3 gr, solution of strychnine hydrochloride 3 m, dilute phosphoric acid 20 m, chloroform water to 1 oz.

**[P1 81] Elixir Ergotæ cum Ferro (Martindale)**

*Dose* —2 drachms, repeated if necessary.

Dissolve soluble iron pyrophosphate 5 gr in 1 dr of warm water and add to liquid extract of ergot 10 m mixed with simple elixir 50 m.

For anæmia and excessive (or diminished) menstruation in young women.

**[P1 81] Tinctura Ergotæ Ammoniata (B P C)**

*Dose* — $\frac{1}{4}$  to 1 drachm (2 to 4 ml) 1 in 4 with 10% of dilute solution of ammonia.

A sample contained 0.02% of alkaloids —*Pharm. J.*, 1/1936, 342.

**[P1 81] Ergometrina (B P. Add)**  $C_{19}H_{23}O_2N_3 = 325.2$  *Syn and Prop. Names.* ERGONOVINE (N N R), ERGOTOCIN, ERGOBASINE, ERGOSTETRINE.

*Dose* — $\frac{1}{120}$  to  $\frac{1}{80}$  grain (0.0005 to 0.001 g), by intramuscular injection,  $\frac{1}{240}$  to  $\frac{1}{120}$  grain (0.00025 to 0.0005 g); by intravenous injection,  $\frac{1}{480}$  to  $\frac{1}{240}$  grain (0.000125 to 0.00025 g).

In colourless, hygroscopic crystals becoming coloured on exposure to air. Two forms occur; one has m.p. 162° to 164° (decomp.), and the other, obtained from acetone, has m.p. 212°.

The low m.p. form is less stable than that with the higher m.p.

*For method of extraction, see Vol II*

**Soluble** readily in alcohol and acetone, sparingly soluble in benzene and chloroform, moderately soluble in water. The aqueous solution has a blue fluorescence and becomes brown on exposure owing to oxidation. Ergometrine differs from other ergot alkaloids in being soluble in water, and almost insoluble in chloroform.

The low m p. form tends to pass into the high m p. form on keeping, and the latter can also be obtained readily by crystallisation in the presence of a crystal of the high m p. variety. The more stable form is less soluble, but both have the same specific rotation.—R. L. Grant and S. Smith, *Nature, Lond.*, 1/1936 154

### Nomenclature of Ergot Alkaloids.

Shortly after the isolation of ergometrine by H. W. Dudley and Chassar Moir (*Brit. med. J.*, 1/1935, 520), three further independent announcements were made of the isolation of a new alkaloid of ergot effective when administered orally. Kharasch and Legault (*J. Amer. chem. Soc.*, 1935, 57, 956, 1140) adopted the name **ergotocin**; Stoll and Burckhardt (*C. R. Acad. Sci., Paris*, 1935, 200, 1680) named their alkaloid **ergobasine**; and M. R. Thompson gave the name **ergostetrine** to the alkaloid previously named by him X-alkaloid (*J. Amer. pharm. Ass.*, 1935, 185, 748). Considerable discussion arose as to the identity or otherwise of these four alkaloids, and as to which name should be adopted for general usage. The case for the adoption of ergometrine was stated by Sir H. H. Dale (*Science*, 11, 1935, 99). Following an interchange of samples of their products, the workers concerned (with H. King in place of the late H. W. Dudley) agreed that the four names were synonymous (see M. S. Kharasch, H. King, A. Stoll and M. R. Thompson, *Nature, Lond.*, 1/1936, 403). Subsequently the Council on Pharmacy and Chemistry of the A.M.A. selected the name **ergonovine** for use in N.N.R. on the grounds that it was not a proprietary name and was not therapeutically suggestive. The product at first named ergotocin is being supplied commercially in America under the name Ergotrate, and ergostetrine is being supplied under the name Ergokline.

**Pharmacology.** Ergometrine differs from other ergot alkaloids by the absence of the paralyzing effect on augmentor sympathetic actions, and by a much weaker activity in the production of gangrene. Its specific action is to initiate a long persistent rhythm of powerful contractions in a uterus normally quiescent, as in the puerperium. If the uterus already exhibits a vigorous spontaneous rhythm, ergometrine does not enhance it. It is more readily absorbed than ergotoxine, but anaesthetized animals differ from the human patient in showing no regularity of response to oral doses of ergometrine which produced immediate effects when given intravenously.—G. L. Brown and Sir Henry Dale, *Proc. roy. Soc., Ser. B*, 1935, 118, 446.

Clinically it is remarkable for rapidity of action which distinguishes it from the ergotoxine-ergotamine group. By mouth,

using average doses, an effect is usually seen in 5 to 8 minutes, by intramuscular injection in from 3 to 4½ minutes, and by intravenous injection in about 1 minute. The onset of action is abrupt, and there is well-marked uterine spasm lasting for about an hour, after which isolated strong contractions occur at regular intervals and continue for 1½ to 3 hours or more (though it is difficult to get exact information on this point). When powerful action is required in the shortest possible time (*e.g.*, in post-partum hæmorrhage) larger doses should be employed, such as, by mouth, 1 mg.; intramuscularly, 0.5 mg.; intravenously, 0.125 mg., though these doses have been increased to as much as 1.5 mg., 0.75 mg. and 0.15 mg. respectively without symptoms of intolerance. It is freer from unpleasant side-effects (depression, headache and nausea) than the ergotoxine-ergotamine group, and from dangerous gangrene-producing properties. While the ergotoxine-ergotamine group is distinctly inferior to ergometrine in rapidity of action, it produces a spasm of longer duration and the total duration of effect is also probably longer. At the same time, the precise duration of action with ergometrine is not a matter of primary importance, since if it is required to keep a long effect it is a simple matter to repeat the administration of ergometrine by an oral dose. In post-partum hæmorrhage it is a serious rival to pituitary extract; although ergometrine does not act so quickly by intramuscular injection it is well suited to intravenous injection, and when given by this route a uterine response appears in about 1 minute. Moreover, it seems to be uniformly reliable and consistent in its action.—Chassar Moir, *Proc. R. Soc. Med.*, 1935, 1663.

[P1 81] **Ergometrine Hydrochloride.** White crystals, soluble in water, m.p. 245° to 246° (decomp.).

[P1 81] **Ergotamine.**  $C_{33}H_{45}N_5O_5$ .

Colourless crystals darkening on exposure to light.

**Soluble** in alcohol 90%, chloroform and acetone, sparingly soluble in ether.

Its pharmacological action is identical with that of ergotoxine but it is a chemically distinct alkaloid. It is available commercially only as the tartrate in the proprietary article Femergin (*vide infra*).

Some discussion has taken place between Prof. Stoll and Drs Smith and Timmis as to the occurrence of ergotamine in ergot of rye, the English workers maintaining that ergotamine is not a normal constituent (*vide Lancet*, ii/1930, 652, 873, 994, 1148).

[P1-81] **Ergotamine Tartrate** is official in *P. Belg. IV* with formula  $(C_{33}H_{45}O_5N_5)_2 \cdot C_4H_6O_6 \cdot 2CH_3OH$ .

**Toxic Effects.** Gangrene of the feet, necessitating amputation of the legs, following hypodermic injections of ergotamine tartrate, in a fisherman suffering from toxæmia with jaundice of unknown ætiology, the injections being given for pruritus. 19 ml. was injected within a week. The drug should probably not be used in cases of febrile puerperium, in severe toxæmia, or in patients who have presented evidence of vascular disease, functional or organic. At the present time the use of the drug should probably be limited by the profession

at large to appropriate obstetric and gynaecologic conditions and to the relief of migraine. Oral use is less likely to produce toxic effects —W M. Yater and J. A. Cobill, *J Amer med Ass*, 1/1936, 1631

Report of a case of gangrene and death in a middle-aged woman following 4 injections (each 0.25 mg.) of ergotamine tartrate for pruritus. The use of drugs of this type should be avoided in cases of vascular disease —S E Gould and co-workers, *J. Amer med Ass*, 1/1936, 1635

**GRAVES' DISEASE** Ergotamine tartrate injections, 1 mg intramuscularly, gave improvement, but not in severe cases. Or subcutaneously  $\frac{1}{2}$  grain each morning, repeated in the evening if tolerated. Suspend for a week or two after 20 to 25 days —*Per Prescriber*, 1929, 391.

**MIGRAINE** treated by ergotamine tartrate, 2 mg daily by mouth, with additional 2 mg. when an attack is threatened —*Per Prescriber*, 1929, 33

Given in 45 cases (6 men and 39 women) it caused abrupt termination of headache in 40. Speed of pharmacological effect varies with route of administration, *e g*, intravenously, relief in 15 to 30 minutes, subcutaneously, 1 to 2 hours; *per os*, 2 to 3 hours. Recommended single dosage 0.5 mg subcutaneously or 1 mg *per os*. Only give half subcutaneous dose at first trial. Injection can be repeated after 2 or 3 hours. For prompt sustained effect 0.25 mg intravenously and at the same time the same amount subcutaneously. Caution advised in hyperpetic subjects and contraindicated in pregnancy. Appears to be without avail in prevention of subsequent attacks, and dangers of ergotism prevent regular administration. —W G. Lennox, *New Engl J Med.*, 1934, 210, 1061

Among the most recent and promising forms of treatment is the intramuscular injection of ergotamine tartrate 0.5 ml. The benefit as to headache is frequently almost dramatic, though it may cause vomiting or uterine colic. The usual effect is to bring promptly to a close an attack which would otherwise disable the patient for hours, or even days —M Critchley, *Brit med J*, 11/1935, 795

**URTICARIA** of vagotonic or sympatheticotonic origin treated with ergotamine tartrate. Dose —2 to 3 mg *per os* daily for 2 to 3 weeks —*Brit. med J Epit*, 11/1929, 44

[P1 81] **Femergin Tablets** (Sandoz, London; Brooks & Warburton, London), contain 0.001 g of ergotamine tartrate. Also supplied in solution for oral use and ampoules for injection

[P1 81] **Ergotinina**.  $C_{22}H_{40}O_5N_2 = 610$  *Syn* ERGOTININE CRYSTALLISÉE (*Fr Cx Supp.*, 1920)

Dose — $\frac{1}{2}$  to  $\frac{1}{4}$  grain (0.0003 to 0.001 g.) *Fr Cx* has the latter as *max single dose*

An alkaloid in minute colourless needles, soluble in 200 of alcohol 95%, less in ether, very soluble in chloroform, insoluble in water.

This alkaloid has been proved to be inert

**Ergine**. A degradation product obtained by the action of methyl alcoholic alkali on ergotoxine and ergotinine

It is the amide of lysergic acid,  $C_{18}H_{17}H_3 COOH$ , which is obtained by the degradation of ergotinine with aqueous alkali —S Smith and G. M Timmis, *Nature*, 1/1934, 579

Clinical tests should be carried out on ergine —G Barger, *Pharm J*, 11/1933, 599

[P1 81] **Ergotoxina** (B P.C.)

Dose. — $\frac{1}{10}$  to  $\frac{1}{5}$  grain.

A white amorphous powder darkening on exposure to light and air.

**Soluble** in alcohol, acetone, chloroform and ethyl acetate, also in benzene, from which it crystallises with 2 molecules of solvent; almost insoluble in water.

It is strongly active physiologically on the uterus—raises blood pressure, and is the principle in ergot that produces gangrene in the cock's comb on injection.

The degree of uterine spasm and its duration after permissible dosage is not so great as has sometimes been supposed. Repeated investigations have shown

that, in the puerperal uterus at least, spasm does not last longer than about an hour and a half after 0.5 mg. of ergotoxine or ergotamine intramuscularly —Chassars Moir, *Proc R Soc Med*, 1935, 1661.

[P1 81] **Ergot Aseptic Ampoules** (*Parke, Davis, London*) Preparation of ergot preserved with Chloretone, for intramuscular injection Dose —1 ml

[P1 81] **Ernutin** (*Burroughs Wellcome, London*) A solution physiologically standardised for hypodermic use, containing ergotoxine, Tyramine and Ergamine (*v. infra*) in two forms (a) for oral use, dose —30 to 60 minims, to be given after labour is completed, every 3 hours until contraction effected, and (b) for hypodermic use, dose —5 to 10 minims, after expulsion of the placenta

[P1 81] **Ergotoxinæ Æthanosulphonas** (*B P*) Probable formula  $C_{35}H_{11}N_5O_6 \cdot C_2H_5 SO_2 OH = 737.5$

Dose. — $\frac{1}{10}$  to  $\frac{1}{100}$  grain (0.0005 to 0.001 g) by subcutaneous or intramuscular injection

Colourless, odourless, acicular crystals containing about 83.6% of ergotoxine

**Soluble** in alcohol 90%; readily soluble in methyl alcohol, sparingly soluble in water

[P1 81] **Ergothane** (*Evans, Sons, Lescher & Webb, Liverpool*) Ampoules of ergotoxine ethanesulphonate solution containing 0.0005 g per ml Dose —0.5 to 1 ml (0.25 to 0.5 mg) intramuscularly or subcutaneously, repeated in 24 hours if necessary

[P1 81] **Ergotoxinæ Phosphas** (*B P C*)

Dose — $\frac{1}{10}$  to  $\frac{1}{100}$  grain (0.0005 to 0.001 g) by subcutaneous or intramuscular injection.

Colourless crystals darkening on exposure to air and light

**Soluble** 1 in 18 of boiling alcohol 90%, less soluble in cold alcohol, sparingly soluble in water

### Other New Ergot Alkaloids.

In addition to the above alkaloids, other new constituents have recently been reported

[P1 81] **Sensibamine** was obtained in 1932 by a method patented by the Chinoïn A G, of Budapest. It decomposes on contact with organic solvents.

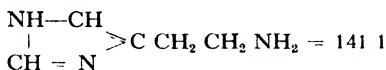
[P1 81] **Ergoclavine** was obtained by W. Kussner (*Arch Pharm, Ber*, 1934, 503) in hygroscopic crystals, resembling sensibilamine but differing from it in being recrystallisable from acetone or alcohol. It is stated to constitute 16 to 20% of the total alkaloids of Spanish and Russian ergots. Probable formula  $C_{31}H_{39}N_5O_6$ .

**Ergoclavine and Sensibamine** are pharmacologically identical with ergotoxine and therefore also with ergotamine —A. Vartiainen, *J Pharmacol*, 1935, 54, 259

[P1 81] **Ergometrine**.  $C_{19}H_{23}O_2N_3$ . Obtained by S. Smith and G. M. Timmis (*Nature, Lond.*, 11/1934, 259). Has no physiological action, and bears the same relationship to ergometrine as ergotamine to ergotamine, or as ergotinine to ergotoxine. It can be converted to ergometrine by treatment with acid.

[P1 81] **Ergosine** and [P1 81] **Ergosinine** are isomeric alkaloids, probably  $C_{30}H_{35}O_5N_5$ , which have been obtained also by Smith and Timmis (*Nature, Lond.*, 1/1936, 111, 1075). The latter is sparingly soluble in water and methyl alcohol but can be recrystallised from aqueous acetone.

**Histamine.** *Syn and Prop Name* AMINOETHYLGLYOXALINE, 4- $\beta$ -IMINAZOLYLETHYLAMINE, ERGAMINE (*Burroughs Wellcome, London*)



A base present in ergot, usually prepared synthetically from protein decomposition products. It is used therapeutically as the acid phosphate.

**Pharmacology.** It has intense action on plain muscle. The plain muscle fibre of the uterus in particular is stimulated to contraction by minute doses. Injected subcutaneously it causes fall of blood pressure, and in other than minimal doses it produces a violent and intense erythema all over the body, headache, conjunctivitis, paræsthesias, vomiting, tenesmus, bronchial spasm and unconsciousness.

**HEADACHE.** Following intravenous injection of 0.1 mg histamine acid phosphate there is an interval while the substance is travelling to the systemic capillaries. At the 20th second there is a metallic taste, the face flushes, systolic and diastolic blood pressures begin to fall and the cerebrospinal fluid pressure suddenly rises. These symptoms progress for 10 to 20 seconds and then pass away. Headache begins about 40 seconds after onset of vasodilation, reaches a maximum in half a minute, lessens a minute later and disappears in 6 to 10 minutes. The indications are that the headache arises from the stretching of the walls of the cerebral arteries or the tissues in their immediate neighbourhood.—G. W. Pickering and W. Hess, *Brit med J*, ii/1932, 1097. See also J. F. O'Malley, *ibid*, 1208.

#### **Histamine in Relation to Blood Pressure.**

Histamine is, no doubt, liberated from the tissues in response to injury. Intravenously in cats a dose of 1 to 2 mg per kilo causes respiratory disease, due to contraction of bronchiolar muscles, and rise of blood pressure, due to contraction of muscles of arterioles. Profound fall of blood pressure follows within 4 or 5 minutes. It has a powerful dilating effect on the smallest vessels. The hypothesis of "Histamine Shock" is that the circulation is brought to a precariously low point by depletion of the central vessels, much rich corpuscular blood remaining locked in the minute vessels and much of its fluid part finding its way into extravascular tissue spaces. Similar effects in man with small intravenous or subcutaneous doses. Larger doses subcutaneously (6 to 8 mg.) cause fall of blood pressure, respiratory distress, contraction of stomach, and occasionally collapse.—"The Blood Vessels of the Human Skin and their Responses," Thomas Lewis (1927), 108-109 (H. K. Lewis).

**Histaminæ Phosphas Acidus** (*B.P. Add*). *Syn* HISTAMINÆ PHOSPHAS (*U.S.P. XI*).  $\text{C}_5\text{H}_9\text{N}_3, 2\text{H}_3\text{PO}_4$  = 307.2

*Dose*— $\frac{1}{150}$  to  $\frac{1}{60}$  grain (0.0005 to 0.001 g.) by subcutaneous injection.

In colourless, odourless, prismatic crystals. **Soluble** 1 in 4½ of water, slightly in alcohol.

**Uses.** Is administered hypodermically, by injection, and by ionisation in the treatment of rheumatism, being especially useful in chronic cases with vasomotor disturbances. Is also useful in chronic rheumatoid arthritis, in osteoarthritis and related conditions, and in pruritus associated with urticaria. Its stimulating action on the production of gastric juice is used in the differential diagnosis of pernicious and secondary anæmias by means of the fractional test meal; in the achlorhydria of pernicious anæmia 0.5 to 1 ml of 1 in 1000 solution does not induce secretion of hydrochloric acid. The 1 in 1000 solution has also been used in the diagnosis of circulatory disturbances such as Raynaud's

disease In normal patients, when the solution is pricked into the skin, a red spot followed by a weal should appear in about 2½ minutes. In Raynaud's disease and allied affections this reaction is delayed.

**ASTHMA.** With suitable technique and individualised dosage, histamine treatment may produce permanent and satisfactory results in bronchial asthma and urticaria. Begin in severe cases with 0.00001 mg. and in milder cases with 0.0001 mg. The first injection is given intracutaneously, and when it causes no noticeable reaction, give the same dose subcutaneously the following day, later injections given at intervals of two days. Doses gradually increased up to a maximum of 0.01 mg.—A. Dzsinich, *Klin. Wschr.*, 11/1935, 1612.

**CHEYNE-STOKES' RESPIRATION.** Normal breathing resumed and continued for about 6 hours after small dose of histamine subcutaneously. Slight headache, feeling of warmth, and occasional reddening of skin of arms and neck—symptoms pass off in an hour. Following two further injections next day Cheyne-Stokes' respiration ceased altogether.—F. Kisch, *Klin. Wschr.*, 1930, 1819, per *Prescriber*, 1930, 655.

**POST-OPERATIVE COLLAPSE.** After the intravenous injection of 0.005 mg. of histamine most persons show a brief fall of the systolic blood pressure, whereas those subject to post-operative circulation disturbances react to such an injection with a fall of blood pressure followed by an often considerable rise. In these latter patients the subcutaneous injection of 0.5 to 1 mg. of histamine twice a day for 8 to 10 days before an operation has been found a valuable prophylactic measure to combat the tendency to post-operative collapse.—S. Rusznyak and co-workers, *Dtsch. med. Wschr.*, 1935, 1111.

**RHEUMATISM.** Histamine given subcutaneously in the form of a solution of strength 1 mg. of histamine acid phosphate in 1 ml. of saline, with 0.5% of phenol. Initial dose 0.1 mg., increased daily by 0.05 mg. till definite improvement observed. Satisfactory dose usually between 0.1 and 0.5 mg., which is repeated 2 or 3 times weekly and further increased if response diminishes. Sensitivity varies: women usually more sensitive than men (but does not affect menstruation). With long intervals between doses (e.g., a week) some increased sensitivity observed. Of benefit in all types of rheumatism, but in particular the type characterised by co-existence of impaired grip, the result of periarticular arthritis in the hand, with vasomotor disturbances (e.g., cold and cyanotic fingers). Cases with gross heart disease or high blood pressure unsuitable. Patients lie down for 15 to 30 minutes after injection to diminish liability to headache and giddiness. The following effects have been observed: flushing, relief of pain, increased range of joint movement, relief of vasomotor symptoms, sweating, headache, dizziness, drowsiness, increased appetite, a sense of well-being, changes in blood pressure and temperature, and paræsthesiæ. Similar results obtained with Thio-histamine intramuscularly, but less potent than histamine. Histamine ionisation effects purely local, apparently the result of local galvanism, heat and counter-irritation. Pain and swelling relieved in all types of cases, often accompanied by flushing and headache, but general therapeutic effects absent.—B. Shanson and C. G. Eastwood, *Lancet*, i/1934, 1226. See also F. S. Mackenna, *ibid.*, 1228, Bissett, *ibid.*, 1366, and Woodmansey and Bissett, *ibid.*, 11/1933, 1018.

**Liquor Histaminæ Phosphatis (U.S.P. XI)**

*Average dose.*—5 minims (0.3 ml.) by parenteral injection. A 0.1% solution of histamine acid phosphate in distilled water.

**Amino-Glucosan** (*Wolm, Spangenberg, Saccharin Corporation, London*) 10% solution of histamine hydrochloride used in the form of eye drops as a miotic in acute glaucoma.

**Apomigran** (*Schwabe, Leipzig*).

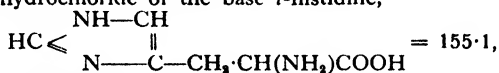
A homeopathic proprietary containing histamine and sodium sulphate. In bile and liver affections.

**Imadyl** (*Hoffmann-La Roche, London*) Histamine preparations in various forms—2% ointment for ionisation (may also be used by massage), also tablets containing 0.05 g (1 tablet to 1 litre for immersion or 1 in 5000 solution for moistening anode pad), ampoules for injection, 1 mg in 1 ml (doses increasing from 0.1 to 0.5 mg).

**Thio-Histamine** (*British Drug Houses, London*) An organic sulphur compound administered by intramuscular injection for the removal of fibrotic lesions resulting from previous inflammation. Also useful in acne rosacea and vulgaris, seborrhoeic and other forms of dermatitis, and in thrombo-angitis obliterans. A course of treatment consists of the injection on three successive days of 0.001 g, 0.002 g, and 0.003 g, no further injections being made for 6 to 8 weeks. The solution may also be applied locally around the lesion twice daily until signs of inflammation occur.

### Histidine Hydrochloride.

**Dose.**—3 grains (0.2 g.), in 4% aqueous solution, given daily for about 3 weeks by subcutaneous or intramuscular injection. The monohydrochloride of the base *l*-histidine,



which is the amino-acid corresponding to histamine

The 4% solution is administered by injection in the treatment of peptic ulcer. Symptomatic improvement usually occurs after 4 or 5 injections. The theoretical basis of the treatment rests on the work of Aron and Weiss (*Pr. méd.*, 1933, 93, 1880), who showed that peptic ulcer could be produced in dogs by preventing duodenal digestion by surgical means. They suggested that ulcer formation was connected with a deficiency of amino-acids and that this deficiency was corrected by the injection of histidine. These experiments have been subjected to serious criticism by H. C. Barry and H. W. Florey (*Lancet*, 11/1936, 728) who, as a result of further experiments on cats and pigs, were unable to substantiate the suggestion of Aron and Weiss.

**PEPTIC ULCER.** Of 18 cases of duodenal ulcer and 4 of gastric ulcer all showed gain or preservation of weight and disappearance of subjective symptoms after 10 to 30 daily injections of 0.2 g. of histidine subcutaneously or intramuscularly in 5 ml. of fluid. In 16, the ulcer previously detected radiologically was found to have disappeared.—G. Hessel, *Munch. med. Wschr.*, 1934, 1890.

Found best for gastric ulcers, and can be employed for ambulant patients without special systematic dietetic restrictions. Average course of 21 injections.—J. W. König, *Schweiz. med. Wschr.*, 1935, 1008.

Relief from symptoms follows as a rule in 2 to 6 days, and some 60 to 90% of cures are recorded. But as most workers point out, it is far too early to assess the value of this treatment. Already some disappointing relapses are known, and there will probably be general agreement that histidine is not a specific remedy for peptic ulcer, in the sense that it does not counteract the cause. If this is so, it must seem unwise to relax attention to dietetic and general measures while carrying out injection treatment. The longest case-histories hitherto reported are less than two years, and the word "cure" is therefore inappropriate to any of them. The time has not yet come for accepting an entirely new theory of ulcer causation and for abandoning the ordinary rules of diet and management.—*Lancet*, i/1936, 95.



Thirty-five cases of peptic ulcer treated with intramuscular injections of a 4% solution of histidine hydrochloride, averaging 24 injections, with no local or systemic reaction. Six patients, 3 with gastric and 2 with duodenal ulcers, with an average history of symptoms of 2½ years, showed immediate clinical and roentgen evidence of cure, with marked gain in weight and no recurrence after 6 months.—J. T. Eads, per *J. Amer. med. Ass.*, 11/1935, 1636.

Favourable results corroborated in 46 cases of gastro-intestinal ulcers—best results in new cases. Oral administration much less effective than parenteral. The incidence of roentgenologically demonstrable cicatrization higher after treatment with histidine monohydrochloride than after the usual therapeutic methods. Average increase in weight 4 to 7 kg.—E. E. Hauke, *Dtsch. med. Wschr.*, 1935, 1510.

Histidine is a specific remedy for peptic ulcer. In chronic appendicitis, cholecystitis, gastritis, and neurotic dyspepsia the results are bound to be disappointing. Similarly, when pyloric stenosis is present no satisfactory results may be expected until the necessary surgical treatment has been carried out. Even cases in which ulcer is undoubtedly present will not do well if complications such as gall-bladder disease or chronic appendicitis are associated with the ulcer. It is very necessary, therefore, that care should be taken in the diagnosis of peptic ulcer.—T. A. Kean, *Med. Pr.*, 1/1936, 363.

Results obtained in 40 patients do not warrant routine injections of histidine in all ulcer patients. The expense involved, the 24 consecutive intramuscular injections, the mild reactions experienced by an appreciable number of patients, the high percentage of recurrences within 6 months after treatment, and the fact that approximately the same percentage of patients respond favourably to the diet-alkali regimen without histidine injections—these speak against the routine use of histidine in ulcer therapy. Histidine produced remission of ulcer symptoms in 55% of the patients treated, it did not prolong the symptom-free interval nor did it prevent recurrences, 85% of the patients who developed remissions have returned with ulcer symptoms within 6 months after treatment. However, histidine may be used as "extra artillery" in patients not responding to the diet-alkali-antispasmodic management. About 50% of the latter patients may thereby become symptom-free and an additional 20% moderately improved.—D. J. Sandweiss, *J. Amer. med. Ass.*, 1/1936, 1459.

Comparison of a series of 41 cases treated with histidine hydrochloride with 40 controls treated with the usual diet-alkali ulcer regimen showed that symptomatic and radiologic response of the patients in the histidine series was not quite as good as that in the diet-alkali series, in either the initial or the sustained effects. The clinical improvement appears to be symptomatic and transient. Chronicity and rhythmicity is a characteristic feature of peptic ulcer. Histidine appears to have no effect other than to alter the rhythm slightly. It showed no constant effect on the hydrochloric acid secretion. The therapeutic indications for histidine in the treatment of peptic ulcer are necessarily limited. The extravagant claims that have been made for this substance are unwarranted.—D. A. Kirby (for Council on Pharmacy and Chemistry of the A.M.A.), *J. Amer. med. Ass.*, 1/1936, 1472.

The treatment should be reserved for simple uncomplicated cases, for cases of stoma-ulcer, and in patients in whom other methods have failed. It should be regarded at present as an adjunct to simple diet-alkali treatment, it is most useful as an ambulatory method, but adequate after-treatment should be enforced on the usual lines.—E. Bulmer, *Lancet*, 1/1936, 734.

**Larostidin** (*Hoffmann-La Roche, London*) and **Stellidin** (*Pharmaceutical Specialties (May & Baker) Ltd, London*) are sterile 4% solutions of L-histidine hydrochloride in 5 ml ampoules for intramuscular or subcutaneous injection.

Larostidin not acceptable for N.N.R. because it is marketed in America with unwarranted therapeutic claims. The Council concluded, however, that although there is at present insufficient clinical evidence for its evaluation, histidine hydrochloride shows promise of possible usefulness in the treatment of gastric and duodenal ulcer.—*J. Amer. med. Ass.*, 1/1936, 1473.

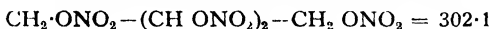
**Tyramina.** *Syn. and Prop. Name.* p-HYDROXYPHENYLETHYL-AMINE, TYRAMINE (*Burroughs Wellcome, London*).  
 $\text{OH} \cdot \text{C}_6\text{H}_4 \cdot \text{CH}_2\text{CH}_2\text{NH}_2 = 137.1.$

*Dose.*— $\frac{1}{2}$  to  $\frac{1}{4}$  grain (0.02 to 0.04 g.) by hypodermic injection of the acid phosphate.

An organic base present in aqueous extracts of ergot but obtained synthetically. Has a weak but prolonged adrenaline action but no local vasoconstrictor effect. It has practically no effect on the uterus. Has been used to raise blood pressure in collapse.

**Methylaminomethyl-heptene.** *Syn* OCRIN. Is a sympathomimetic amine which stimulates the respiratory centre and, to a lesser degree, other parts of the central nervous system. With carefully adjusted dosage a great rise of arterial pressure is produced which may not fall to normal for 2 to 3 hours. It is markedly slower in action than adrenaline.—D. E. Jackson, *J. Pharmacol.*, 1935, 54, 152.

## ERYTHRITYLIS TETRANITRAS



*Syn* ERYTHROL TETRANITRATE, NITRO-ERYTHRITE, ERYTHRO-TETRANITRAL, ERYTHROL NITRAS

[P1] "*Erythrityl tetranitrate*"

**Dose** — $\frac{1}{2}$  to 1 grain (0.03 to 0.06 g.), increased to 3 grains or more in tablet form *vide infra*. When erythrityl, or erythrol, tetranitrate is prescribed, twice the prescribed amount of diluted erythrityl tetranitrate must be dispensed.

In colourless and slightly tar-like smelling crystals, m.p. 61°. The crystals are explosive unless mixed with an inert diluent. **Soluble** in water about 1 in 20,000, about 1 in 60 of absolute alcohol. It is formed by dissolving erythrol (a sugar obtained from various lichens, e.g., *Rocella tinctoria*, *R. fuciformis*, etc.), in fuming nitric acid, and precipitating by sulphuric acid.

**Uses.** As a vasodilator. Its slight solubility as against that of glyceryl trinitrate (1 in 800) renders its action in reducing blood pressure slower and more prolonged. It is employed in angina pectoris, chronic Bright's disease, nephritis, aneurism, arteriosclerosis, Raynaud's disease, dyspnoea, headache and nervous affections accompanied by high blood pressure. It is often effective in the paroxysms of asthma, especially if followed by a hot drink, and in relieving the spasms of lead colic. For angina, to avert paroxysms, even half a drachm a day has been taken. Præcordial pains are promptly relieved by one tablet 3 times a day.

Daily use of the tablets, beginning with  $\frac{1}{2}$  grain thrice daily and gradually increasing, will ward off attacks. Cumulative effect or tolerance has not been observed. Erythrityl tetranitrate produces little effect until half an hour after its administration, and the maximum effect is produced at the end of an hour, the arterial tension gradually increases again, but it does not return to its previous condition until about 10 hours after the dose has been taken.

**PRURITUS.** Of 21 cases of generalised pruritus, complete relief was obtained in 10 and moderate relief in 7 by the use of erythrityl tetranitrate by mouth in doses of 0.03 g. and glyceryl trinitrate in tablets containing 0.0006 g. Effect possibly associated with dilatation of the cutaneous vessels. Of no value in localised pruritus.—Prinzmetal, *Arch. Derm. Syph.*, N.Y., 1934, 843.

[P1] **Erythritylis Tetranitras Dilutus** (B.P., U.S.P. XI). *Syn.* ERYTHRITYL TETRANITRATE (50%), ERYTHROL TETRANITRATE (50%).

*Dose.*— $\frac{1}{2}$  to 2 grains (0.03 to 0.12 g.) representing  $\frac{1}{4}$  to 1 grain (0.015 to 0.06 g.) of pure erythrityl tetranitrate U.S.P. average dose (of dilution) 5 grains.

A mixture of approximately equal weights of erythrityl tetranitrate and lactose, the latter being added in order to minimise the risk of explosion.

[P1] **Tabellæ Erythritylis Tetranitratis Diluti** (B.P.C.)

Contain 1 gr. (0.06 g.) in chocolate basis.

[P1] **Tabellæ Sodii Nitritis Compositæ** (B.P.C.).

*Dose.*—1 or 2 tablets.

Each tablet contains sodium nitrite  $\frac{1}{2}$  gr., diluted erythrityl tetranitrate  $\frac{1}{2}$  gr. and ammonium hippurate 1 gr.

[P1] **Mannitylis Hexanitras**. *Syn.* HEXANITRIN, NITROMANNITE, MANNITOL NITRATE.  $\text{CH}_2\cdot\text{ONO}_2\cdot(\text{CH}\cdot\text{ONO}_2)_4\cdot\text{CH}_2\cdot\text{ONO}_2$ —452.1

*Dose.*— $\frac{1}{4}$  to 1 grain (0.016 to 0.06 g.) increased.

The nitrate of the hexahydric alcohol, mannite,  $\text{C}_6\text{H}_8(\text{OH})_6$ —182.1. In light acicular crystals, m.p. 113°, practically insoluble in water. Is used similarly to erythrityl tetranitrate but is more explosive and requires extra care. In angina and asthma its action is not so powerful, but probably more prolonged.

[P1] **Tabellæ Mannitol Nitratis** (Martindale)

Contain 1 grain (0.06 g.) in chocolate basis.

## EUONYMUS

### B.P.C.

The dried root-bark of *Euonymus atropurpureus* (Celastraceæ), the wahoo or spindle-tree.

*Uses.* Possesses tonic, hydragogue cathartic, diuretic and anti-periodic properties.

**Elixir Euonymi et Pulsatillæ** (B.P.C.).

*Dose.*—1 to 4 drachms (4 to 16 ml.).

Tincture of euonymus 12.5, tincture of pulsatilla 12.5, simple elixir to 100.

**Extractum Euonymi** (B.P.C.). *Syn.* EUONYMIN.

*Dose.*—1 to 2 grains (0.06 to 0.12 g.). Tablets,  $\frac{1}{4}$ ,  $\frac{1}{2}$  grain  $\frac{1}{4}$  to 1 grain cholagogue, 1 to 4 grains cathartic.

A brown alcoholic extractive containing calcium phosphate to keep it as powder. In commerce chlorophyll is sometimes added. *Fr. Cx.* has Euonymine Brune, *max. single dose*,  $1\frac{1}{2}$  grains 1 grain, combined with 4 grains of iridin, is a successful purge.

**Extractum Euonymi Liquidum.**

1 = 1, made with alcohol (90%) 4, water 1. *Dose.*—10 to 60 minims (0.6 to 4 ml.).

**Liquor Euonymini et Iridini (B.P.C.).**

*Dose.*— $\frac{1}{2}$  to 1 drachm (2 to 4 ml.).

Contains the equivalent of about 3.5% *w/v* of extract of euonymus and 2% *w/v* of extract of iris.

**Liquor Euonymini et Pepsini (B.P.C.).**

*Dose.*— $\frac{1}{2}$  to 1 drachm (2 to 4 ml.).

Contains 1 gr. of extract of euonymus and 2 gr. of pepsin in 1 dr.

**[P1] Pilula Euonymini.**

Euonymin 2 gr., extract of hyoscyamus  $\frac{1}{2}$  gr., for 1 pill, taken at bedtime. A cholagogue stimulant, producing no depression or headache, requires to be followed by a saline aperient in the morning

**Tinctura Euonymi (B.P.C.).**

*Dose.*—10 to 40 minims (0.6 to 2.6 ml.) 1 in 5 of alcohol 45%

**Iridis Rhizoma (B.P.C., P. Helv. V)** *Syn.* ORRIS ROOT. The rhizome of *Iris germanica*, *I. pallida* and *I. florentina* (Iridaceæ) Contains "concrete oil of orris" or "butter of orris" (0.1 to 0.2%), used in perfumery, and irone,  $C_{13}H_{20}O$ , an oil with pungent odour, violet-like in very high dilution. Irone for use in perfumery is prepared synthetically from citral.

**Iris (B.P.C.),** *syn* BLUF FLAG, is the dried rhizome and roots of *I. versicolor*, and contains a cathartic resinoid.

**Extractum Iridis (B.P.C.).** *Syn.* IRIDIN.

*Dose.*—1 to 3 grains (0.06 to 0.2 g.) in pills, often with extract of hyoscyamus or euonymus. A dry extract prepared with alcohol 70%, and mixed with calcium phosphate to reduce caking

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**EXTRACTUM FELLIS BOVINI****B.P.*****Syn.* FEL BOVINUM PURIFICATUM**

*Dose* —5 to 15 grains (0.3 to 1 g.) in enteric-coated capsules or pills.

A dark yellowish-green, bitter-sweet mass

**Soluble** in water and alcohol 90%, insoluble in ether.

**Manufactured** by evaporating 20 of fresh ox bile to 5, mixing with 10 of alcohol 90%, separating the precipitate and evaporating the clear fluid to thick extract consistence. It is composed of bile salts, cholesterin, lecithin and bile pigments. Capsules contain 5 grains.

**Uses.** An emulsifier of fat and a stimulant to the action of the liver. Has been given in jaundice and typhoid. A small quantity diluted with water may be used as an enema in obstinate constipation

Dysentery has been treated with satisfactory results by rectal injection of  $1\frac{1}{2}$  to 2 oz. of fresh bile of sheep.

**Extractum Felle Bovis (U.S.P. XI)** *Average Dose*—6 grains (0.4 g.) A dry extract adjusted with starch so that 1 g. represents 8 g. of ox bile

**Fel Bovinum Exsiccatum.** *Dose*—5 to 10 grains in cachets

Fel Bovis (U.S.P. XI) is the fresh bile of the ox

**Sodii Tauroglycocholas (B.P.C.)** *Syn* BILE SALTS

*Dose*—2 to 6 grains (0.12 to 0.4 g.), preferably in capsules

A yellowish-brown hygroscopic powder consisting chiefly of sodium taurocholate,  $C_{26}H_{44}O_7NSNa$ , and sodium glycocholate,  $C_{26}H_{42}O_6NNa$ . **Soluble** 2 in 1 of water, and in alcohol, insoluble in ether. It is prepared by extracting pig or ox bile with dehydrated alcohol, decolorising, and precipitating with ether. Is cholagogue, and assists pancreatic digestion.

**ACUTE ILEUS.** Human bile used successfully in 9 out of 13 cases. Freshly secreted human bile from a cholecystectomy preferable, but can be kept in an ice-chest for a week. Give 2 oz. of bile in 4 oz. of saline per rectum and repeat every 4 hours until definite improvement is seen and bowels have been opened, reverting to bile if vomiting returns. Causes no discomfort and no difficulty in retention. Only water, orange juice, and glucose allowed until ileus is overcome. Both ox bile and vomited human bile have also been used, but both cause acute pain and are not so effective as fresh human bile.—R. St. Leger Broekman, *Lancet*, 11/1927, 320

**Acute intestinal obstruction.** The action of human bile often dramatic.—*Lancet*, 1/1929, 442

**Sodii Desoxycholas.**  $C_{24}H_{39}O_4Na = 414.3$  Obtained from the tauroglycocholate by alkaline hydrolysis and crystallisation from glacial acetic acid of the separated bile acids. A white soluble powder, very irritating when inhaled. Bile salts appear to possess a solvent action on pneumococci, also on amebæ and spirochaetes. The addition of quinine enhances the action.

**SPRAY SOLUTION.** Sodium desoxycholate 4, quinine hydrochloride 0.5, glycerin 25, water to 100. For septic throats.

**TABLETS.** Contain sodium desoxycholate 1 gr., quinine ethyl carbonate  $\frac{1}{2}$  gr., peppermint oil  $\frac{1}{2}$  m., ammoniated glycyrrhizin 2 gr. Also made with acriflavine 1 in 1000. For infected throats.

**Sodii Glycocholas.**  $C_{26}H_{42}O_6NNa = 487.3$

*Dose*—2 to 6 grains (0.12 to 0.4 g.)

A similar salt prepared from the lead salt precipitated from a tauroglycocholate solution by lead acetate. **Soluble** 1 in 2 of water and 1 in 3 of alcohol 90%. Appears to be a useful cholagogue for congestion of the liver, gall-stones, constipation and melancholia.

These salts produce slight fall of blood pressure, the taurocholate more than the glycocholate.

Bile salts are the only certain cholagogues.—Sir Humphrey Rolleston, *Lancet*, 1/1925, 1207

**CHOLECYSTITIS.** Sodium glycocholate 3 gr. with hexamine 7 gr. in cachets, 1 night and morning.—W. Bain, *Lancet*, 1/1929, 495

**MIGRAINE.** Good results in 22 patients following use of bile salts, capsules of sodium glycocholate being given in doses of 2 to 20 gr. *t.d.s.*, investigations showing that many cases of migraine are caused through errors of the biliary mechanism.—T. C. Hunt, *Lancet*, 11/1933, 279

**Sodii Taurocholas.**  $C_{26}H_{44}O_7NSNa = 537.4$

*Dose.*—2 to 6 grains (0.12 to 0.4 g.), in pill, keratin-coated to prevent solution until it reaches the bowels.

A whitish powder, separated from the filtrate of the precipitation of tauroglycocholate with lead acetate **Soluble** about 2 in 1 of water. It has been recommended for gouty obesity and dyspepsia.

**Lotio Sodii Taurocholatis (BVH)** Sodium taurocholate 1½ dr., oil of eucalyptus 1 oz., water to 20 oz. For pediculosis. The taurocholate emulsifies the oil and assists penetration of the louse's egg.

The following are proprietary preparations containing bile salts advocated for the treatment of constipation and liver disorders:—  
[P1 87] **Cholasa** (*Organotherapeutic Laboratories, Osnabruck, Braun, London*) Tablets containing decomposition product from liver albumin, pituitary (posterior lobe) extract, magnesium glycocholate, magnesium oleate, hexamine, podophyllin, and oil of peppermint.

**Decholin** (*Riedel-de Haen, Berlin, Old Strand Chemical and Drug Co., London*) Consists of dehydrocholic acid, a powerful cholagogue. In tablets containing 0.25 g. or in ampoules containing 10 ml. of 20% solution of the sodium salt. **Dose**—Of tablets, 2 thrice daily.

Powerful stimulant (warn patient) to bile excretion and probably also to the liver cells themselves.—T. C. Hunt, *Lancet*, ii/1930, 1002.

While sodium dehydrocholate has some diuretic effect it becomes a satisfactory diuretic in most cases only when combined with Salyrgan. The effective dosage of Salyrgan seems to be considerably lower when used in this combination, the maximum output following administration of 1 ml. or less of Salyrgan with simultaneous intravenous injection of 10 ml. of 20% sodium dehydrocholate. Sodium dehydrocholate intravenously is contraindicated in mechanical obstruction of the bile passages, acute hepatitis and acute yellow atrophy.—F. A. Weigand, *J. Amer. med. Ass.*, ii/1935, 2034.

**Degalol** (*Riedel-de Haen, Berlin, Old Strand Chemical Co., London*) Desoxycholic acid and menthol. **Dose**—1 or 2 tablets thrice daily.

**Felagol** (*Richter, London*) Tablets containing sodium cholate 2 gr., hexamine salicylate 2½ gr., benzyl succinate ½ gr., lactic ferments ½ gr., oil of peppermint ¼ gr. **Dose**—2 tablets thrice daily.

**Felamine** (*Sandoz, London, Brooks & Warburton, London*) Hexamine glycocholate in tablets containing 5 gr. (0.3 g.). Cholagogue and biliary antiseptic. In catarrhal jaundice, constipation and enteritis and in the after-treatment of typhoid fever and for gallstones.

**Glandulax** (*Richter, London*) Tablets of biliary salt, pancreas, duodenum, digestive ferments, pectin and aloin. **Dose**—2 to 3 daily.

**Lactobyl** (*Continental Laboratories, London*) Tablets containing biliary salts, intestinal glands, hyperactivated charcoal, lactic ferments and extract of lamnaria.

**Oleoformine** (*Corbière, Paris, Anglo-French Drug Co., London*) Combination of cholic acid, sodium oleate and hexamine in gluten-coated tablets. **Dose**—3 to 4 tablets twice daily in acute cases, 2 tablets twice daily in chronic cases.

**Opobyl** (*Bengué, London*) Contains hepatic and biliary extracts, extracts of boldo and combretum, podophyllin and euonymin. For hepatic and biliary insufficiency.

**Pancrobilin** (*Reed & Carnick, New Jersey, Coates & Cooper, London*) Pills (or liquid) containing pancreatic enzymes and bile salts. [P1 81]

**Compound** pills contain in addition ½ gr. of strychnine, ½ gr. of belladonna and ½ gr. of aloin.

**Sal-Cholate** (*Lilly, London*) Tablets containing sodium glyco- and taurocholate ½ gr., sodium salicylate 1½ gr., phenolphthalein ½ gr., extract of cascara sagrada ½ gr. **Dose**—1 or 2 at bedtime or 1 after each meal.

**Suprachol** (*Richter, London*) Sodium dehydrocholate in ampoules of 10 ml. of 5% or 20% solution for intravenous injection, and in 4-grain tablets.

**Taxol** (*Laboratoires Lobica, Paris, Continental Laboratories, London*) Tablets containing powdered intestinal mucosa 0.05 g., biliary extracts 0.10 g., agar 0.05 g., lactic ferments 0.05 g.

**Veracolate** (*H. R. Warner, London*) Tablets containing sodium glycocholate ½ gr., sodium taurocholate ½ gr., extract of cascara 1 gr., phenolphthalein ½ gr., oleoresin of capsicum ½ gr.

**Boldo (B.P.C.).**

*Dose.*—1 to 3 grains in cachet or capsule. The dried leaves of *Peumus Boldo* (Monimiaceæ) from Chili and Bolivia. They resemble those of Sweet Gale (*Myrica Gale*), but are more aromatic. In dyspepsia, liver affections, rheumatism, and as a diuretic for atony of the bladder.

**Tinctura Boldo (B.P.C.).** 1 in 10 of 60% alcohol.

*Dose.*—10 to 30 minims (0.6 to 2 ml.). The natives of South America take half a litre of strong decoction a day for hepatic diseases.

**Boldine Houdé** (*Laboratoires Houdé, Paris, Wilcox, Jozeau, London*) Granules containing 1 mg of the alkaloid holdine *Dose*—3 to 6 granules daily In hepatic disorders

**FERRUM**

Fe = 55.84.

**Ferrum (B.P.).** Consists of iron wire of 0.1 mm diameter *U.S.P. XI* requires it to be in form of fine bright wire, filings, or powder.

**Extractum Ferri Pomatum** (*P.G. VI, P. Ital. V*) is prepared by digesting iron filings in juice of sour apples, and contains 5% of iron

**Tinctura Ferri Pomata** (*P.G. VI*) *Dose*—15 to 30 minims (1 to 2 ml.) Ferrated extract of apples 1 part, cinnamon water (*P.G. VI*, containing 10% of alcohol) 9 parts.

**Liquor Ferri Acetatis.**

*Dose.*—5 to 15 minims (0.3 to 1 ml.).

Prepared by dissolving freshly precipitated ferric hydroxide in acetic acid and diluting with glycerin and water.

Pneumonia has been treated with full doses every 6 hours until crisis past.

**Solutio Ferri Subacetatis** (*P. Helv. V*) is a similar preparation adjusted to contain 5% of Fe.

**Liquor Ferri et Ammonii Acetatis.**

*Average dose.*—4 drachms (15 ml.)

Tincture of ferric chloride 4, dilute acetic acid 6, solution of ammonium acetate 50, aromatic elixir 12, glycerin 12, water to 100. To be freshly made. Useful in anæmia and particularly in chronic parenchymatous nephritis. It acts as a good diuretic and diaphoretic.

**Mistura Ferri Acetatis** (*W.H.*). *Syn.* BASHAM'S MIXTURE

Solution of ferric chloride 15 m, solution of ammonium acetate 2 dr, dilute acetic acid 15 m, glycerin 15 m., water to  $\frac{1}{4}$  oz. For chronic parenchymatous nephritis.

**Ferrum Redactum** (*B.P., U.S.P. XI*) *Syn.* QUEVENNE'S IRON.

*Dose.*—1 to 10 grains (0.06 to 0.6 g.). *U.S.P. XI* average dose 8 grains.

Fine powdered iron containing at least 80% (*U.S.P. 90%*) of metallic iron, prepared by reducing ferric oxide with hydrogen.

*P. Dan* and *P. Helv. V* include both Ferrum reductum and Ferrum pulveratum.

**Incompatible** with tannin and metallic salts.

Pills of Reduced Iron require  $\frac{1}{4}$  to  $\frac{1}{2}$  grain of compound tragacanth powder to bind them.

**Trochisci Ferri Redacti** (*B.P.C.*) contain 1 grain

**Vinum Ferri** (*B.P.C.*).

*Dose*.—1 to 4 drachms (4 to 16 ml.).

Sherry-type wine in which iron has been immersed until the liquid contains 0.125 to 0.300% *w/v* of Fe.

**Ferri Carbonas Saccharatus** (*B.P., P. Helv. V*)

*Dose*—10 to 30 grains (0.6 to 2 g.).

Ferrous oxycarbonate,  $\alpha\text{FeCO}_3 \cdot y\text{Fe}(\text{OH})_2$ , partially oxidised and mixed with liquid glucose, the mixture containing not less than 50% of ferrous iron calculated as  $\text{FeCO}_3$ . *P. Ital. V* requires 9.5 to 10.5% of Fe.

**Incompatible** with tannin-containing drugs, also with acids and acid salts

**Uses.** For anæmia and chlorosis of young women

**Mistura Ferri Composita** (*B.P.C.*) *Syn.* GRIFFITH'S MIXTURE

*Dose*— $\frac{1}{2}$  to 1 ounce (15 to 30 ml.)

Contains ferrous carbonate equivalent to about 3 gr. of ferrous sulphate per oz.

**Pilula Ferri Carbonatis** (*B.P.*) *Syn.* BLAUD'S PILL, PILULA FERRI, IRON PILL, MASSA FERRI CARBONATIS (*U.S.P. XI*).

*Dose*.—5 to 30 grains (0.3 to 2 g.) *U.S.P. XI* average dose 4 grains

Each 5 grains contain about  $\frac{1}{2}$  grain of iron.

**ANÆMIA** Massive iron therapy—up to 60 gr. of Blaud's pill daily—the most effective treatment of secondary anæmia. Ferrous better than ferric salts—*Lancet*, 11/1931, 531

In the treatment of MICROCYTIC HYPERCHROMIC ANÆMIAS it is usually a waste of time, material, and money to give less than 45 gr. of Blaud's pill or 60 gr. of iron and ammonium citrate daily in the early stages—J. F. Wilkinson, *Practitioner*, 11/1933, 418

In SPLENIC ANÆMIA, whether it is believed that operation is indicated or not, treatment with effective doses of iron—iron and ammonium citrate 90 gr. daily, Blaud's pill 45 gr. daily, ferrous sulphate, chloride or carbonate in tablet form, 9 gr. daily—should be tried for at least 6 to 8 weeks before iron therapy is held to have failed—L. S. P. Davidson, *Lancet*, 11/1934, 596.

In the treatment of HELMINTHIC ANÆMIA, iron in large doses (Blaud's pills 3 to 4 tds and iron and ammonium citrate 1½ to 2 grammes tds) combined with a well balanced diet (fats and proteins) proved most effective. Iron was found more effective in ankylostoma anæmia than in that due to intestinal bilharziasis. Liver therapy proved ineffective.—M. Salah, *per Trop. Dis. Bull.*, 1936, 33, 151.

COMBINED DEGENERATION OF THE CORD successfully treated by Blaud's pill 150 gr. daily, in capsules. Liver treatment may be necessary in addition—W. Sargant, *Lancet*, 1/1932, 232.

Details of a further case successfully treated with massive iron therapy—J. B. Snowman, *Lancet*, 1/1932, 613.



COMBINED SCLEROSIS Treatment by massive iron therapy gave uniformly good results, but relapses result if Blaud's pill is reduced to below 40 or 50 gr a day —W Sargent, *Brit med J*, 11/1933, 34

**Pilulæ Ferri Carbonatis** (*U.S.P. XI*) Average dose —3 pills

Each pill contains about 1 gr of  $\text{FeCO}_3$

**Pilulæ Ferri Carbonatis Compositæ** (*B.P.C.*) *Syn*  
BLAUD'S PILL WITH ALOIN AND CASCARA

Dose.—1 to 3 pills.

Contain 5 gr. of pill of iron carbonate with  $\frac{1}{10}$  gr. of aloin and  $\frac{1}{4}$  gr. of dry extract of cascara sagrada.

[P181] **Pilulæ Ferri Carbonatis cum Arseno et Strychnina**  
(*B.P.C.*). *Syn* BLAUD'S PILL WITH ARSENIC AND STRYCHNINE

Dose.—1 or 2 pills

Contain 5 gr. of pill of iron carbonate with  $\frac{1}{100}$  gr of arsenic trioxide and  $\frac{1}{100}$  gr of strychnine hydrochloride

[P181] **Pilulæ Ferri Carbonatis et Arseni** (*B.P.C.*) *Syn*  
BLAUD'S PILL WITH ARSENIC

Dose —1 pill

Contain 5 gr of pill of iron carbonate and  $\frac{1}{10}$  gr of arsenic trioxide

**Pilulæ Ferri Carbonatis Saccharati** (*B.P.C.*)

Dose —1 to 3 pills

Contain 3 gr. of saccharated iron carbonate per pill, equivalent to about 10 gr of Blaud's pill

**Tabellæ Ferri Carbonatis** (*B.P.C.*)

Dose —1 to 6 tablets

Contain the equivalent of 5 gr of Blaud's pill

**Tabellæ Ferri Carbonatis et Aloini** (*B.P.C.*) *Syn* BLAUD'S  
TABLETS WITH ALOIN

Dose —1 to 6 tablets.

Contain the equivalent of 5 gr. of Blaud's pill and  $\frac{1}{10}$  gr of aloin

**Ferri Citras.**

Dose —5 to 15 grains (0.3 to 1 g)

Contains ferric citrate corresponding to not less than 16% of Fe  
Garnet-red soluble scales with slight ferruginous taste

**Ferri et Ammonii Citras** (*B.P. Add, U.S.P. XI*)

Dose —20 to 40 grains (1.3 to 2.6 g) 40 grains contains about  
8 grains of iron *B.P.* '32 gave max dose 15 grains *U.S.P. XI*  
average dose 30 grains Contains 20.5 to 22.5% (*B.P.*) or 16%  
to 18.5% (*U.S.P. XI*) of metallic iron Dark red scales soluble  
in about half their weight of water Is also available in granules.

In debility and anemia Especially preferred in lingering cases  
of gastric catarrh after alkalis have ceased to benefit and the  
stomach is not ready for an acid tonic Also with sodium salicylate  
in subacute rheumatism of children

In ANEMIA OF CHILDREN had no appreciable effect —N K Gibbs, *Lancet*,  
11/1929, 550

Simple achlorhydric anemia treated by iron and ammonium citrate 90 gr.  
daily increased to 120 gr —D C Hare, *Brit. med J*, 11/1931, 889

CHLOROSIS in young persons well treated by iron Chronic microcytic anæmia in mid-life treated by iron and ammonium citrate, 60 to 120 gr. daily for 4 to 5 months —L. J. Wits, *Lancet*, 1/1931, 146

Anæmia is prevalent among nearly half the women of the poorest classes in Aberdeen, and appears to be mainly due to increased demands for iron as a result of frequent pregnancies, or of excessive blood loss during menstruation and/or parturition The anæmia can be rapidly cured with marked improvement of general health by administration of iron salts. It is suggested that a glass of milk and a pennyworth of iron and ammonium citrate, without any other change in the diet of pregnant women of the poorest classes, would produce remarkably beneficial results to mother and infant —L. S. P. Davidson and co-workers, *Brit. med. J.*, 1/1933, 689

**Mist. Ferri et Ammon. Cit. (N I F)** Iron and ammonium citrate 10 gr., ammonium carbonate 1 gr., chloroform water to  $\frac{1}{2}$  oz

[P1] **Mist. Ferri Cit. c. Arsen. (N I F)** Iron and ammonium citrate 7½ gr., arsenical solution 3 m., chloroform water to  $\frac{1}{2}$  oz

**Vinum Ferri Citratis (B P C)**

Dose —1 to 4 drachms (4 to 16 ml.) (contains about 1 gr. of iron and ammonium citrate per drachm of orange wine)

**Ferri et Ammonii Citras Viridis (B P C)** *Syn* FERRI ET AMMONII CITRATES VIRIDES (*U S P XI*)

Dose —5 to 10 grains (0.3 to 0.6 g.) Hypodermically  $\frac{1}{2}$  grain in 4% w/v solution, but for this purpose it must be neutralised with ammonia to give no red colour with either methyl red or phenol red

*U S P XI* average dose, by parenteral injection, 1 grain

Green deliquescent scales prepared as for iron and ammonium citrate but using more acid and sufficient ammonia to give a green colour Contains 14 to 16% of Fe

**Injectio Ferri (B P)**

Dose —15 to 30 minims (1 to 2 ml.) 30 m. contains the equivalent of about  $\frac{1}{15}$  gr. of iron

Contains a double citrate of iron and ammonium

The injection tested in 10 cases. It was found to be of very low therapeutic efficiency owing to the small proportion of iron, and also painful, but this could be corrected by adding 3% of procaine hydrochloride Double the maximum official dose can be given, but would have to be given twice daily for 6 weeks to equal the effect of large oral doses. Except in rare instances the administration of iron by the parenteral route should be avoided —G. N. Burger and L. J. Wits, *Proc. R. Soc. Med.*, 1934, 27, 447

Iron given by injection is quite inert, the popular and expensive ampoules of such solutions may have some effect on the mind, but they have none on the blood. When 30 gr. of iron and ammonium citrate is given thrice daily, the hemoglobin generally increases by about 1% a day. It is unsafe to give much larger doses. 40 gr. 4 times a day for 3 weeks may cause acute iron encephalopathy —A. E. Hurst, *Pharm. J.*, 11/1934, 675

[P1 S1] **Injectio Ferri et Arseni (B P C)**

Dose —8 to 15 minims (0.5 to 1 ml.) intramuscularly Contains the same proportion of iron as *Injectio Ferri* together with  $\frac{1}{10}$  gr. of arsenic trioxide per 15 m.

[P1 S1] **Arsen-Electroferrol** (*Heyden, Dresden, Braun, London*) Colloidal iron and arsenic solution containing 0.05% of Fe and 0.025% of As for intravenous injection in anæmia

[P1 S1] **Ferarin** (*Squire, London*) Solution of green iron and ammonium citrate with arsenic for intramuscular injection

[P1 S1] **Ferri et Ammonii Citro-Arsenis (B P C)** *Syn.* SOLUBLE IRON ARSENIFF

**Dose.**— $\frac{1}{40}$  to  $\frac{1}{2}$  grain (0.0015 to 0.03 g.); maximum daily dose 1 grain (0.06 g.).

A double salt of ferrous arsenite and ammonium citrate in greenish deliquescent scales containing about 14% of Fe and 1.4% of  $\text{As}_2\text{O}_3$ . May be administered by injection.

**Ferri et Ammonii Tartras.**

**Dose.**—5 to 15 grains (0.3 to 1 g.). In garnet-red soluble scales containing not less than 13% of Fe.

**Ferri et Mangani Citras (B.P.C.)**

**Dose.**—3 to 15 grains (0.2 to 1 g.).

In reddish scales, freely soluble in water, containing not less than 14% of Fe and not less than 7% of Mn. Useful in chlorosis, combining the action of the two elements.

**Ferri et Potassii Tartras (B.P.C.).** *Syn* FERRUM TARTARATUM.

**Dose**—5 to 10 grains (0.3 to 0.6 g.).

Reddish-brown scales soluble in water about 1 in 1, very sparingly soluble in alcohol 90%. Contains not less than 20% of Fe.

Menorrhagia of young females is well treated by this tartrate.

For mucous disease, this or the ammonio-citrate is given with alkali in infusion of calumba.

**Ferri Iodidum (B.P.C.).**  $\text{FeI}_2 = 309.7$ . *Syn* FERROUS IODIDE

**Dose.**—1 to 5 grains (0.06 to 0.3 g.).

Crystalline grey or brown hygroscopic masses readily soluble in water.

Mostly prescribed as one of the following—

**Liquor Ferri Iodidi (B.P.C.).** *Syn* LIQUOR PRO SYRUPO FERRI IODIDI

**Dose.**—2 to 8 minims (0.12 to 0.5 ml.)

Contains about 53.5% *w/v* of  $\text{FeI}_2$ , and when mixed with 7 volumes of syrup forms Syrupus Ferri Iodidi.

**Syrupus Ferri Iodidi (B.P.C., P. Ned V)** *Syn*. SIRUPUS FERROSI IODIDI CONCENTRATUS I A.

**Dose.**— $\frac{1}{2}$  to 2 drachms (2 to 8 ml.).

Contains 5% *w/w* of  $\text{FeI}_2$ , 2 drachms contains about  $7\frac{1}{2}$  gr. of ferrous iodide equivalent to about  $1\frac{1}{2}$  gr. of iron.

*P. Belg. IV* and *F.E. VIII* have this strength as concentrated syrups, which diluted 10 times provide dilute syrups containing 0.5% of ferrous iodide. *P. Ital. V* has the same dilute syrup only

**Incompatible** with alkalis such as sal volatile.

**Syrupus Ferri Iodidi (U.S.P. XI)**

**Average dose**—15 minims (1 ml.)

Approximately the same composition and strength as *B.P.* syrup, except that it contains 50% more hypophosphorous acid

**Syrupus Ferri Bromidi (B.P.C.)**

**Dose.**— $\frac{1}{2}$  to 1 drachm (2 to 4 ml.).

Contains about  $4\frac{1}{2}$  gr. of ferrous bromide in 1 dr.

**Syrupus Ferri Bromidi cum Quinina (B.P.C.).**

*Dose.*— $\frac{1}{4}$  to 1 drachm (2 to 4 ml.).

Contains about  $\frac{1}{10}$  gr. of quinine dihydrobromide and 4 gr. of ferrous bromide in 1 dr.

**[P1] Syrupus Ferri Bromidi cum Quinina et Strychnina (B.P.C.).**

*Dose.*— $\frac{1}{4}$  to 1 drachm (2 to 4 ml.).

Similar to the preceding, containing also  $\frac{1}{4}$  gr of strychnine per dr.

**Ferri Oxalas.**  $\text{Fe}(\text{COO})_2 \cdot 2\text{H}_2\text{O} = 179.9$  *Syn.* FERROUS OXALATE, PROTOXALATE OF IRON, FERROSUM OXALICUM (*P. Belg. IV*).

*Dose.*—1 to 5 grains (0.06 to 0.3 g)

Yellow crystalline powder, insoluble in water but soluble in dilute acids. Has been given in anæmia and as a nerve tonic

**Ferri Oxidum Calcinatum.** *Syn.* FERRI SESQUIOXIDUM. Obtained by roasting precipitated oxide of iron, and usually contains about 94% of  $\text{Fe}_2\text{O}_3$ . Impure forms are Armenian bole, ochre, Venetian red, jewellers' rouge, etc

**Ferri Oxidum Magneticum.** *Syn.* FERROSO-FERRIC OXIDE, BLACK OXIDE OF IRON. Occurs as an iron ore, and is obtained by precipitation from a solution of ferrous and ferric salts. Insoluble in water

**Ferri Oxidum Præcipitatum Fuscum (B.P.C.)** *Syn.* FERRI PEROXIDUM.

*Dose.*—5 to 15 grains (0.3 to 1 g) A brown powder containing 80 to 90% of  $\text{Fe}_2\text{O}_3$ .

**[P1 & 83] Emplastrum Ferri (B.P.C.)** *Syn.* EMPLASTRUM ROBORANS, STRENGTHENING PLASTER. Contains 9% of brown precipitated ferric oxide in Burgundy pitch and plaster of lead

**Ferri Oxidum Præcipitatum Rubrum (B.P.C.)** *Syn.* FERRI CARB., FERRI SUBCARB.

*Dose.*—5 to 15 grains (0.3 to 1 g)

Obtained by precipitating ferrous sulphate solution with sodium carbonate and washing and drying the precipitate. A dull brownish-red powder.

**Ferrum Oxydatum Saccharatum (P. Austr., P.G. VI, P. Helv. V, P. Dan.).**

*Dose.*—10 to 40 grains (0.6 to 2.5 g.).

Dilute ferric chloride solution (*P.G. VI*—10% of Fe) 30 g with water 150. Then add with stirring a solution of sodium carbonate 26 in water 150 (towards the end of the precipitation before each fresh addition of the alkali wait for the re-solution of the precipitate). Wash to free from chloride, collect on cloth, press slightly, mix in porcelain dish with powdered sugar 50 and so much sodium hydroxide solution (sp. gr. 1.17) as is required to dissolve on a water-bath (not more than 5 to be used), evaporate, dry, and mix with sugar *q.s.* to make 100.

A reddish-brown powder containing 2.8 to 3% of Fe.

**Ferri Peptonas.** A compound of iron and peptone with addition of sodium citrate to render it soluble. Usually administered as the solution in the treatment of anæmia, neurasthenia and chlorosis.

**Liquor Ferri Peptonatis (B P C)** *Syn* SOLUTION OF PEPTONISED IRON.

*Dose* —1 to 4 drachms (4 to 16 ml)

Contains 0.65% *w/v* of iron and 4% *w/v* of peptone

**Liquor Ferri Peptonatis cum Mangano (B P C)** *Syn* SOLUTION OF PEPTONISED IRON WITH MANGANESE

*Dose* —1 to 4 drachms (4 to 16 ml.)

Similar to the above, but containing also  $\frac{1}{2}$  gr of manganese chloride per drachm

**Liquor Ferri Albuminati (P G VI, P Helv. V)**

*Dose* —1 to 4 drachms (4 to 16 ml)

A solution containing a compound of iron and egg albumen adjusted to contain about 0.4% of Fe. *P. Ned. V* contains 0.25% of  $\text{Fe}_2\text{O}_3$

[P181] **Arsenoferratin** (*Boehringer, Mannheim, Pharmaceutical Products, London*) Arsenic-iron-albumen product, containing 6% of Fe and 0.06% of As. Supplied in 4-grain tablets. *Dose* —1 to 3 tablets 3 or 4 times daily

[P1] **Arsenoferratose.** 5% solution of Arsenoferratin. *Dose* — $\frac{1}{2}$  to 1 tablespoonful 3 or 4 times daily

**Fer Ascoli** (*Allen & Hanbury's, London*) An organic compound of iron with nuclein in tablet form. Used in treatment of anæmia

**Ferratin** (*Boehringer, Mannheim, Pharmaceutical Products, London*) Sodium ferroalbuminate, containing 6% of iron. Tablets contain 4 grains. *Dose* —2 tablets 3 or 4 times daily. **Ferratose.** 5% solution of Ferratin. *Dose* —1 tablespoonful 3 or 4 times daily

[P1] **Ferroarsine** (*Parke, Davis, London*) Solution of iron peptonate and manganese with arsenic peptonate  $\frac{1}{10}$  gr and strychnine sulphate  $\frac{1}{10}$  gr. *Dose* —1 to 2 fluid drachms (4 to 8 ml) thrice daily

**Triferrin** (*Knoll, Ludwigshafen, Pharmaceutical Products, London*) An iron compound of paranucleic acid containing 15 to 16% Fe, 9% N, and 2 $\frac{1}{2}$ % P in organic combination. A rapidly absorbed iron compound undissolved by the gastric juice. In tablets of 5 gr and powder. *Dose* —1 tablet, increased to 3, thrice daily.

**Ferri Perchloridum (B P C, P Helv. V)** *Syn* FERRI SESQUICHIORIDUM, FERRUM SESQUICHIORATUM  $\text{FeCl}_3 \cdot 6\text{H}_2\text{O}$  270.3

*Dose.* — $\frac{1}{2}$  to 2 grains (0.03 to 0.12 g), or more

Deliquescent yellow masses made by evaporating the strong solution and crystallising

**Incompatible** with infusions, etc., containing tannin, with the alkalis, alkaline carbonates, iodides, salicylates and mucilage of acacia. With potassium iodide in presence of potassium citrate a potassium ferricitrate is formed, and hence it is compatible.

**Soluble** in water, alcohol, ether and glycerin

**Uses.** Internally as hæmatinic, externally as astringent and styptic

**BRONCHITIS** The irritating dry cough may be relieved by applying a mixture of 120 gr. of ferric chloride in 2 oz. of glycerin, on cotton wool, wound round a bent probe, which is passed just to the side of the middle line as near the back of the tongue as possible into each vallecula in turn — E. P. Poulton and F. A. Knott, *Practitioner*, 1/1936, 30

**Garg. Ferri Perchlor.** (*N I F*) Solution of ferric chloride 2 dr., potassium chlorate 2 dr., glycerin  $\frac{1}{2}$  oz., water to 8 oz. Dilute with 1 or 2 parts of water

**Glycerinum Ferri Perchloridi** (*B P C.*). Solution of ferric chloride 1, glycerin 1. For use as a paint. Glycerin and chloroform water cover its metallic astringent taste

**Gossypium Stypticum.** *Syn* GOSSYPIUM FERRI PERCHLORIDI. Saturate absorbent wool 85 with water 100 containing ferric chloride 15, and dry. Linteum Stypticum is made similarly

**Liquor Ferri Dialysatus** (*B P C*)

*Dose* —10 to 30 minims (0.6 to 2 ml)

A colloidal solution of ferric hydroxide containing the equivalent of 3 to 4% of Fe. *P Helv V* contains about 3.5% of Fe

A well-tolerated, non-astringent hæmatinic. To be prescribed undiluted or mixed with glycerin.

**Glycerinum Ferri Dialysati.**

Solution of dialysed iron 1, glycerin 2. Keeps well and is palatable

*Dose* —1 drachm (4 ml).

Dialysed iron is useful as an antidote to arsenic—much superior to the moist peroxide, 1 ounce doses should be given repeatedly, preceded by a dose of common salt or sodium bicarbonate

**Colliron** (*Etans, Sons, Lescher & Webb, Liverpool*) 10% solution of colloidal iron

**Idozan** (*Serpens, Copenhagen, Coates & Cooper, London*) 5% solution of colloidal iron. *Dose* —1 drachm, increased to  $\frac{1}{2}$  ounce, thrice daily

**Ovoferri** (*A C Barnes, Philadelphia, Fassett & Johnson, London*) Colloidal iron tonic (1 dr. = 1 gr. of colloidal iron). *Dose* —One tablespoonful in water or milk

**Liquor Ferri Oxychloridi** (*B P C*) *Syn.* SOLUBIF PEROXIDE OF IRON

*Dose* —10 to 30 minims (0.6 to 2 ml)

Contains the equivalent of about 3% w/v of Fe.

**Liquor Ferri Perchloridi** (*B P*).

*Dose* —5 to 15 minims (0.3 to 1 ml)

Contains about 15% of  $\text{FeCl}_3$ , equivalent to about 5% of Fe.

A solution of the same strength may be obtained by diluting 1 volume of Liq. Ferri Perchlor. Fort. with water to 4 volumes.

The use of iron salts applied as a lotion, compress or wet dressing should be discouraged in all vesicular, bulbous and exudative dermatoses. Two cases of permanent pigmentation following the application of 5% ferric chloride solution for the treatment of ivy poisoning —E F Traub and J S Tennen, *J Amer med Ass*, 1/1936, 1711

**ERYSIPELAS** Liq. Ferri Perchlor. 20 or 25 m. thrice daily acts almost as a specific. Collodion locally helps —*Brit med J*, 1/1920, 352

**TINEA CIRCINATA** An intractable case quickly cured, after failure of iodine, salicylic acid and chrysarobin —J H Boulbee, *Brit med J*, 11/1932, 180

**Liquor Ferri Chloridi** (*U.S.P. XI*).

*Average dose* —1½ minims (0.1 ml)

A solution containing 10 to 11% w, w of iron, and from 3 to 5% w/w of HCl, and therefore approximately double the strength of Liquor Ferri Perchloridi (*B P*) Liquor Ferri Perchloridi Fortis

(*B.P.C.*) diluted with an equal volume of water would give a solution of approximately the same iron content.

**Liquor Ferri Sesquichlorati** (*P.G. VI*) contains 10% of Fe approx. **FERRUM SESQUICHLORATUM SOLUTUM** (*P. Helv. V*) is similar.

**Liquor Ferri Perchloridi Fortis** (*B.P.C.*). Contains 20% Fe. Has sp gr. about 1.43. It is four times the strength of **Liquor Ferri Perchloridi**.

[P1] **Mist. Arsen. Ferri et Strych.** (*N.I.F.*) Solution of strychnine hydrochloride 3 m., arsenical solution 3 m., solution of ferric chloride 10 m., dilute hydrochloric acid 1 m., syrup  $\frac{1}{2}$  dr, water to  $\frac{1}{2}$  oz

[P1] **Mist. Ferri et Strych.** (*N.I.F.*). Solution of strychnine hydrochloride 3 m., solution of ferric chloride 10 m., chloroform water to  $\frac{1}{2}$  oz

**Mistura Ferri Salina** (*U.C.H.*).

Potassium citrate 22 gr., solution of ferric chloride 24 m., chloroform water to 1 oz. The styptic taste of iron is masked in this mixture, as a double decomposition occurs between the iron and the potash salt

**Nebula Ferri Perchloridi** (*T.H.*). Ferric chloride 5 gr., glycerin 15 m., water to 1 oz.

**Pigmentum Ferri Perchloridi** (*T.H.*) contains 1 to 2 dr of ferric chloride per oz. of water.

**Tinctura Ferri Perchloridi** (*B.P.C.*)

*Dose.*—5 to 15 minims (0.3 to 1 ml.).

A 25% dilution of strong solution of ferric chloride with diluted alcohol. Is the same strength as **Liquor Ferri Perchloridi**

Owing to the fact that ferric chloride does not remove any of the acid of the gastric juice (as when reduced iron or Blaud's pills are given), this is preferred by many. Thread-worms are killed by rectal injection of 1 dr of the tincture in 10 oz of water. Angio-neurotic oedema has been treated with drachm doses repeated if necessary every 20 minutes

**CUTANEOUS ERYSIPELAS** An old effective remedy is local application of strong solution of ferric chloride, also internal use of tincture of ferric chloride — E. T. Larkham, *Brit. med J.*, 1/1921, 36

**Tinctura Ferri Chloridi** (*U.S.P. XI*)

*Average dose.*—10 minims (0.6 ml.).

Solution of ferric chloride (*U.S.P.*) 35 ml diluted with sufficient alcohol to produce 100 ml.

**Ferri Phosphas** (*B.P.C.*).

*Dose.*—5 to 10 grains (0.3 to 0.6 g.)

A slate-blue amorphous powder consisting of hydrated ferrous phosphate, ferric phosphate and some hydrated iron oxide, containing not less than 47% of ferrous salts calculated as  $\text{Fe}_2(\text{PO}_4)_2 \cdot 8\text{H}_2\text{O}$ .

**Liquor Ferri Phosphatis** (*B.P.C.*).

*Dose.*—4 to 8 minims (0.5 to 2 ml.).

One volume mixed with seven volumes of syrup forms **Syrupus Ferri Phosphatis**.

**Liquor Ferri Phosphatis Compositus** (*B.P.C.*).

*Dose.*—8 to 30 minims (0.5 to 2 ml.)

One volume mixed with seven volumes of syrup forms a compound syrup similar to Syrupus Ferri Phosphatis Compositus.

[P1] **Pilulæ Ferri Phosphatis cum Quinina et Strychnina** (B.P.C.). *Syn.* PILULÆ TRIUM PHOSPHATUM, EASTON'S PILLS.

*Dose.*—1 or 2 pills. Contain saccharated iron phosphate, quinine and strychnine equivalent to  $\frac{1}{2}$  dr of Syrupus Ferri Phosphatis cum Quinina et Strychnina.

Also made twice this strength. Either may be combined with arsenic trioxide,  $\frac{1}{15}$  grain (0.001 g.).

**Syrupus Ferri Phosphatis** (B.P.C.).

*Dose.*— $\frac{1}{2}$  to 1 drachm (2 to 4 ml). Contains 1 g. of anhydrous ferrous phosphate per drachm. Is best prepared, as required, from Liquor Ferri Phosphatis.

**Syrupus Ferri Phosphatis Compositus** (B.P.).

*Syn.* CHEMICAL FOOD, PARRISH'S SYRUP, PARRISH'S FOOD

*Dose.*— $\frac{1}{2}$  to 2 drachms (2 to 8 ml.).

Contains iron equivalent to 0.9% w/v of  $\text{Fe}_2(\text{PO}_4)_2$ , and calcium equivalent to 1.4% w/v of  $\text{Ca}_3(\text{PO}_4)_2$ . 2 dr. contains about  $1\frac{1}{2}$  gr. of anhydrous ferrous phosphate equivalent to about  $\frac{1}{2}$  gr of iron.

**Syrupus Ferri cum Mangano** (Gt Orm H). (*Dose* for 1-year-old child.)

Copper sulphate  $\frac{3}{4}$  gr., manganese chloride  $\frac{1}{4}$  gr., compound syrup of ferrous phosphate to 1 dr

[P1] **Syrupus Ferri Phosphatis cum Quinina et Strychnina** (B.P.). *Syn.* EASTON'S SYRUP, SYRUPUS TRIUM PHOSPHATUM

*Dose.*— $\frac{1}{2}$  to 1 drachm (2 to 4 ml.).

Contains iron equivalent to 1.8% w/v of  $\text{Fe}_2(\text{PO}_4)_2$ , 1.09% w/v of anhydrous quinine, and 0.0246% w/v of strychnine. 1 dr represents 1 gr of anhydrous ferrous phosphate,  $\frac{1}{4}$  gr. of quinine sulphate and  $\frac{1}{15}$  gr of strychnine hydrochloride. It contains only about half the strychnine content of the B.P. 1914 syrup.

A widely-used tonic preparation.

**Liquores pro Syrupo Eastonii.** It is not possible to prepare solutions so that 1 part of the solution containing the iron and 1 part of that containing the alkaloids, when diluted with 6 parts of syrup, will yield an Easton's syrup identical with that of the B.P. By using Liquor Ferri Phosphatis (*see above*) in conjunction with Liquor Quininae et Strychninae a very close approximation is obtained.

[P1 S1] **Liquor Quininae et Strychninae** (B.P.C.). A syrup differing from Syrupus Ferri Phosphatis cum Quinina et Strychnina (B.P.) only in the presence of 0.75% v/v of hypophosphorous acid may be made by mixing 1 oz of this solution, 1 oz of solution of ferrous phosphate,  $\frac{1}{2}$  oz of glycerin, and 1 oz. of distilled water with sufficient syrup to produce 8 oz

[P1] **Syrupus Triplex** (B.P.C.)

*Dose.*— $\frac{1}{2}$  to 1 drachm (2 to 4 ml)

Equal parts of Easton's syrup, Parrish's syrup and compound syrup of hypophosphites.



[P1] **Tabellæ Ferri Phosphatis cum Quinina et Strychnina** (*B.P.C.*), *syn* EASTON'S TABLETS, **TABELLÆ TRIUM PHOSPHATUM**, *dose*—1 tablet, are approximately equivalent to 1 dr of Easton's syrup. Tablets are also made equivalent to  $\frac{1}{2}$  dr

[P1] **Tabellæ Phosphatum et Hypophosphitum Compositæ** (*B.P.C.*), *syn* TRIPLE SYRUP TABLETS, *dose*—1 tablet, are approximately equivalent to 1 dr of triple syrup

**Ferrodic** (*Allen & Hanburys, London*) Chocolate-flavoured granules containing ferrous phosphate and glucose 1 dr = 10 gr of Blaud's pill or 4 dr of Syrup Ferri Phosph Co *Dose*— $\frac{1}{2}$  to 2 teaspoonfuls thrice daily after meals

**Ferrophytin** (*Ciba, London*) Neutral colloidal iron salt of inositol hexaphosphoric acid Pills contain  $\frac{1}{4}$  gr of iron and  $\frac{1}{2}$  gr of phosphorus *Dose*—1 or 2, 3 or 4 times a day Also supplied in granules

### **Ferri Phosphas Saccharatus** (*B.P.C.*)

*Dose*.—5 to 10 grains (0.3 to 0.6 g.).

A slate-blue powder containing hydrated ferrous phosphate with ferric phosphate and iron oxide, the ferrous iron content being not less than 60%, calculated as  $\text{Fe}_3(\text{PO}_4)_2 \cdot 8\text{H}_2\text{O} = 501.7$

**Ferri Pyrophosphas**,  $\text{Fe}_4(\text{P}_2\text{O}_7)_3$ , may be obtained as a white insoluble powder by interaction of ferric sulphate and sodium pyrophosphate When Ferri Pyrophosphas is prescribed Ferri Pyrophosphas Solubilis is always required

**Ferri Pyrophosphas Solubilis** (*B.P.C.*) *syn* FERRI PHOSPHAS SOLUBILIS, SODIO-CITRO-FERRIC PYROPHOSPHATE, FERRUM PYROPHOSPHORICUM CUM AMMONIO CITRICO (*P. Helv. V*)

*Dose*—2 to 8 grains (0.12 to 0.5 g.)

Green soluble scales containing not less than 10% of Fe *P. Helv. V* requires 15.5 to 17% of Fe Darkens on exposure to light

**Ferri Subchloridi Citratum** (*B.P. Add.*). CITRATED FERROUS CHLORIDE

*Dose*.—3 to 5 grains (0.2 to 0.3 g.)  $\text{FeCl}_2 = 126.7$

A buff-coloured powder with astringent, acid, metallic taste Contains not less than 68% of ferrous iron calculated as  $\text{FeCl}_2$ , together with citric acid in an amount equal to one-tenth the proportion of ferrous chloride It is prepared by dissolving iron in hydrochloric acid, assaying, adding the requisite amount of citric acid, evaporating and drying at  $80^\circ$

**Soluble** 1 in 1 of water almost entirely

**Uses.** A convenient method of administering ferrous iron, since the aqueous solution does not readily become oxidised

Metallic iron, colloidal ferric preparations, and the scale preparations, in which the iron is in a complex form and not readily ionised, all require to be given in large doses to produce effects. The soluble ferrous salts are the most active The average effective dose of ferric chloride must be higher than 400 mg of iron a day, equivalent to Liq Ferri Perchlor 40 minims *t.d.s.* Ferric chloride is less potent than ferrous chloride or ferrous sulphate, but is effective if given in sufficient amounts. It is

possible that iron is not absorbed in the ferric valency, and that ferric salts are reduced to the ferrous state in the alimentary tract before absorption. If minimum effective doses of ferrous iron are prescribed, between 50 and 100% of the dose ingested may be utilised for hæmoglobin formation. Reticulocyte crises and repair of anæmia may be observed with a daily dosage as low as 22 mg of ferrous iron by mouth. There now seems no doubt that the effective dosage of preparations of iron is directly proportional to the ease with which they yield free ferrous ions—L. J. Witts, *Lancet*, 1/1936, 1.

**Copper and Manganese as Adjuvants to Iron.** In anæmia, experiments show that while pure uncontaminated iron is ineffective, the addition of small amounts of copper, germanium, nickel, arsenic or manganese make it effective—the results being essentially the same with all the supplementary elements. A large number of other elements tried with negative results—V. C. Myers and H. H. Beard, *J. Amer. med. Ass.*, 11/1929, 1210. See also Prof. A. J. Clark, *Pharm. J.*, 1/1932, 511.

Treatment of 150 cases of anæmia with (1) copper, (2) manganese, (3) copper and manganese, (4) various combinations of copper, manganese and iron, led to the belief that the best treatment was adequate doses of iron in suitable form without any further adjuncts—J. F. Wilkinson, *Brit. med. J.*, 11/1932, 367.

#### **Syrupus Ferri Chloridi.**

Reduced iron 24 gr. is placed in a loosely-covered 6 oz. bottle with dilute hydrochloric acid 1 oz. The solution is filtered and diluted with syrup to 6 oz. Each fluid drachm contains about  $\frac{1}{2}$  gr. of iron. It should be stored away from sunlight or in brown bottles—G. H. W. Lucas and V. E. Henderson, *J. Canad. med. Ass.*, 1933, 298.

**Endomin Tablets** (Reed & Carnrick, New Jersey, Coates & Cooper, London). A proprietary containing iron 8 mg., copper 0.6 mg., manganese 0.4 mg., zinc 0.3 mg., nickel 0.03 mg., cobalt 0.03 mg. and sodium germanate 0.05 mg. Dose—1 to 3 tablets thrice daily. For use in anæmia in conjunction with a palatable easily-digested diet, rich in vitamins.

**Ferro-Constans** (Richter, London) and **Ferronyl** (Napp, London) are tablets of ferrous chloride 0.05 g.

#### **Ferri Sulphas** (B.P., U.S.P. XI, P. Helv. V, P. Dan.)

$\text{FeSO}_4 \cdot 7\text{H}_2\text{O}$  - 278.0. Syn. FERROUS SULPHATE.

Dose—1 to 5 grains (0.06 to 0.3 g.)

In clear, pale, bluish-green crystals containing about  $\frac{1}{2}$  of their weight of iron.

A saturated solution with some crystals of the salt in excess keeps better than a weak solution, in the latter oxidation soon takes place.

**Soluble** 1 in  $1\frac{1}{2}$  of water, insoluble in alcohol 90%.

Is administered in the treatment of chlorosis in young females in 4-grain doses. May give results in 6 weeks—Prof. J. A. Gunn, *Lancet*, 1/1931, 146.

**Mist. Ferri Aperiens** (N.I.F.). Ferrous sulphate 3 gr., magnesium sulphate 40 gr., dilute sulphuric acid 5 m., copper sulphate  $\frac{1}{2}$  gr., peppermint water to 1 oz.

#### **Mistura Ferri Aperiens** (U.C.H.)

Magnesium sulphate 30 gr., ferrous sulphate 2 gr., dilute sulphuric acid 2 m., peppermint water to 1 oz.

**Ferri Sulphas Exsiccatus** (*B.P., P. Helv. V, P. Dan., P. Jap. IV.*).

*Dose.*— $\frac{1}{2}$  to 3 grains (0.03 to 0.2 g.).

Ferrous sulphate dried at 40°; it contains not less than 80% of  $\text{FeSO}_4$ . 5 grains = 7.3 gr. of the crystals.

**Pilula Ferri Sulphatis** contains 3 or 5 grains of exsiccated ferrous sulphate with syrup *q.s.* Dissolving slowly, these pills do not derange the stomach. If made with lanolin or kaolin ointment as excipient they will not crack.

[P181] **Pil. Ferri et Aloin** (*N.I.F.*) Exsiccated ferrous sulphate  $1\frac{1}{2}$  gr., potassium bicarbonate 1 gr., dry extract of *nuxvomica*  $\frac{1}{2}$  gr., dry extract of belladonna  $\frac{1}{2}$  gr., aloin  $\frac{1}{2}$  gr.

**[P181] Pilulæ Ferri et Arseni** (*B.P.C.*). *Syn.* PILULÆ FERRI ARSENICALES.

*Dose.*—1 pill.

Contain 3 gr. of exsiccated ferrous sulphate and  $\frac{1}{10}$  gr. of arsenic trioxide.

[P181] **Pilulæ Ferri Arsenicales cum Strychnina** are the same with  $\frac{1}{80}$  gr. of strychnine hydrochloride per pill.

**Ferrous Sulphate Tablets G.L.** (*Glaxo Laboratories, London*) Desiccated ferrous sulphate equivalent to 1 gr. of ferrous iron and  $\frac{1}{10}$  gr. each of copper and manganese. *Dose.*—Three 3-grain tablets daily. In secondary anæmia.

**Vionase** (*Wilcox, Jozeau, London*) Tablets containing exsiccated ferrous sulphate 2.73 gr., medicinal yeast 2.5 gr., manganese hypophosphite 0.03 gr., copper sulphate 0.015 gr. *Dose.*—1 tablet thrice daily after meals. Anæmia and debility.

**Liquor Ferri Persulphatis** (*B.P.C.*). A solution containing ferric sulphate equivalent to 14 to 15% of Fe.

**Liquor Ferri Tersulfatis** (*U.S.P. XI*).

A solution of ferric sulphate containing 9.5 to 10.5% *w/w* of iron. Sp. gr. about 1.43 at 25°.

**Liquor Ferri Subsulphatis.** *Syn.* MONSEL'S SOLUTION.

*Dose.*—3 to 6 minims (0.2 to 0.4 ml.).

A solution of basic ferric sulphate. When evaporated and scaled forms **Monssel's Salt** or **Ferric Subsulphate**  $\text{Fe}_2\text{O}(\text{SO}_4)_2$ .

*Dose.*— $\frac{1}{2}$  to 2 grains (0.03 to 0.12 g.).

A spray of 20 grains to the ounce checks hæmoptysis, and internally is not irritating although astringent.

[P181] **Unguentum Ferri Persulphatis** (*General Hosp., Notts*) Ferric sulphate 10 gr., almond oil  $\frac{1}{2}$  dr., conium ointment to 1 oz.

The name persulphate may be taken to mean normal ferric sulphate,  $\text{Fe}_2(\text{SO}_4)_3$ , as contained in **Liquor Ferri Tersulphatis** (*U.S.P. XI*).

**FILIX MAS**

*B.P., P. Helv. V, P. Dan*

*Syn.* ASPIDIUM (*U.S.P. XI*), MALE FERN.

*Dose.*—1 to 3 drachms (4 to 12 g.).

The dried rhizome and leaf-bases of *Dryopteris Filix-mas*, collected late in the autumn, divested of the roots and dead

portions, and not older than one year from the date of collection.

**Dangers** of filix mas. Moderate doses almost invariably produce bilirubinæmia and large doses jaundice. There is risk of chronic cirrhosis of the liver developing.—O Hannsen, *Lancet*, 11/1922, 1188

. About 100 cases of serious impairment of vision have been reported following administration of filix mas, mostly in South Germany and Switzerland.—*Per J. trop. Med. (Hyg.)*, 1925, 168.

**Antidotes.** Give purgative dose of magnesium or sodium sulphate. Demulcent drinks, but avoid oils and fats. Stimulants. Keep patient warm.

**Extractum Filicis (B.P.).** *Syn.* EXTRACTUM FILICIS LIQUIDUM, LIQUID EXTRACT OF MALE FERN, OLEORESINA ASPIDII (U.S.P. XI).

**Dose.**—45 to 90 minims (3 to 6 ml.). *U.S.P. XI* average dose, once a day, 1 drachm (caution). Larger doses, up to 2 or 3 drachms, are sometimes given.

Prepared by ether extraction—the yield being about 9 to 10%—and adjustment with olive oil to contain 25% of filicin, the anhydride of filicic acid, stated to be inactive as a vermifuge.

*P. Ital V* requires 20 to 28% of crude filicin, *F.E. VIII* 24 to 25%, *P. Belg. IV* 24%, *U.S.P. XI* not less than 24%.

**Prescribing Note.** The taste of this preparation is very unpleasant. It is best prescribed in a capsule or, if in a draught, it may be emulsified with an equal weight of acacia or tincture of quillaia, and flavoured with an essential oil such as cinnamon.

**Uses.** For all varieties of tapeworm and *ankylostomum duodenale*. May be administered fasting, and should be preceded and followed by a brisk purgative. The following routine has been successful in obstinate cases. Light food at tea-time—purgative at bedtime (magnesium sulphate and jalap suitable), purgative again in morning, after action give vermifuge. After passage of the worm give castor oil to remove remaining vermifuge from the bowel. **Note**—Castor oil is not advised *before* or *with* a filix mas preparation, since it aids absorption.

Two preliminary doses of sodium sulphate at 5 and 8 p.m. on the previous day and a water enema in the morning. Then an emulsion of extract of filix mas and infusion of senna with acacia through a duodenal tube. Dose of extract 6 ml. for adult to 2 ml. for child of 5†.—*Brit. med. J. Epit.*, 11/1929, 62.

When all other methods fail, the following is often successful: Pumpkin seed 8 g., koussou 4 g., pomegranate 4 g., made into an infusion, to which is added kamala 4 g., oleoresin of aspidium 4 g., glycerin 15 ml., mucilage of acacia 15 ml., water to 240 ml. Give in two draughts 2 hours apart, after usual preliminary treatment. Severe gastro-enteric irritation with vertigo and prostration may result, but it usually gets the worm. Or give by duodenal tube into an empty stomach the morning after a day's preparation with milk diet and a cathartic, half a dose of a senna infusion (5 in 100), and 15 minutes later 2 g. of oleoresin of aspidium and 4 g. of extract of pomegranate seed mixed with the other half of the senna infusion. Remove tube promptly. Whole worm expelled in ½ to 2 hours. No treatment of any kind for tapeworm should be repeated at a less interval than three months.—*J. Amer. med. Ass.*, 11/1928, 585.

**Hauftus Filicis (W.H.).** Extract of male fern 1 dr., syrup of ginger 30 m., mucilage of acacia 2 dr., peppermint water to 1 oz.

**Hauftus Filicis Maris (L.H.).** Liquid extract of male fern 1 dr., syrup of ginger 1 dr., tincture of quillaia ½ dr., peppermint water to 1 oz.

**Mistura Filicis** (*Gt. Orm. H.*). (Dose for children 2 years old and upwards).  
Extract of male fern  $\frac{1}{2}$  dr, spirit of cinnamon 4 m, syrup 2 dr, mucilage of  
acacia 1 dr, chloroform water to  $\frac{1}{2}$  oz

**Filicin.** *Syn* FILICIC ACID

May be extracted on the lines of the chemical assay of the liquid extract  
It is a combination of various acid bodies and is soluble in ether and slightly  
soluble in alcohol

The dose of filicin, if given, may be stated as from 5 to 15 grains

An investigation on flatworms and tapeworms showed it to be an excellent  
helminthicide the ingested filicin reaches the intestine, impregnates the tænia,  
passes into the blood and then into the bile and returns to the intestines, where  
it again acts on the parasites—this cycle being repeated many times The drug  
is given in pills or capsules (in oil solution) in 12-grain doses for adults, and to  
children  $\frac{1}{2}$  grain for each year of age There are no toxic effects if given in  
suitable doses Tænia are stated to be expelled in a few hours Combined with  
calomel both an anthelmintic and purgative action is obtained —*Brit med J*  
*Epid.*, 1/1927, 20.

**Aspidinofilicinum Oleo Solutum** (*PG VI*) *Syn* ASPIDINOLFILIZINOL  
A 10% solution in a neutral vegetable oil

**Filmaron-Oil 10%** (*Boehringer, Mannheim, Pharmaceutical Products,*  
*London*) Dose —8 5 to 20 g *per os*, children 3 to 7 g As an enema (following  
a wash-out enema) in oxyuriasis, 10 g in an equal quantity of oil

**Kamala** (*BPC*) *Syn* GLANDULA ROHLER4

Dose — $\frac{1}{2}$  to 2 drachms (2 to 8 g)

The hairs and glands obtained from the fruits of *Mallotus*  
*philippinensis* (*Euphorbiacæ*) Contains rottlerin and resins  
Used as an anthelmintic against tapeworm, being administered  
in honey, gruel or mucilaginous suspension Its administration  
should be preceded by the administration of sodium bicarbonate  
for 48 hours

**Mucuna** (*BPC*) *Syn* COWHAGE, COWITCH

Dose —10 to 60 grains (0 6 to 4 g) The hairs covering the  
fruit of *Mucuna pruriens* (*Leguminosæ*) Mixed with honey or  
treacle, it can be used as a tænicide

## FORMALDEHYDUM (LIQUOR)

*B.P., USP XI, P. Belg IV, Fr Cx, P Jap, P Helv V,*  
*FE VIII, P Ital V*

*Syn* FORMALIN, FORMOL, METHYL ALDEHYDE SOLUTION

The synonym formalin may be used only in *Gt Britain* and  
*Northern Ireland*. In other countries this name is registered as a  
trade-mark.

[P2] "Formaldehyde."

[B3] "Formaldehyde—in substances containing less than 5%, weight  
in weight, of formaldehyde ( $\text{HCHO}$ ); photographic glazing or  
hardening solutions"

Dose.—1 minim, internally, well diluted

An aqueous solution containing 37 to 41% *w/v* of formaldehyde,  
 $\text{HCHO} = 30.02$ . Is prepared by the catalytic oxidation of  
methyl alcohol. Some methyl alcohol is stated to be left in the

product in order to prevent polymerisation. Sp gr 1.080 to 1.095  
*P. Jap* has also Aqua Formalinata 1 in 35 of the 35% preparation

**Caution** According to the *B.P.C.* a 1% solution of formalin and a 1% solution of formaldehyde both mean 1% of the pharmacopœial 40% solution. If it is desired to indicate the strength of actual formaldehyde, error is avoided by using the chemical formula, e.g., 1% of  $\text{HCHO}$

**Antidotes.** Empty stomach by emetic. Give repeated 1 dr doses of aromatic spirit of ammonia, or  $\frac{1}{2}$  dr dilute solution of ammonia in  $\frac{1}{2}$  pint water. Demulcent drinks

Poisoning of a boy, aged 7, treated by washing out the stomach and then giving a quantity of very dilute ammonia, as an attempt to produce hexamine with the formaldehyde. An uneventful recovery was made.—*Brit med J*, 11/1927, 687

**Uses.** An active antiseptic preventing fermentation and decomposition. Useful for sterilising surgical instruments and the hands of operators. Has been suggested, 1 or 2%, as a pigment and spray for diphtheria. Also as glycerin pigment 2% to the throat in angina follicularis, and as a lotion in pertussis 2% or less—with caution. For alopecia 10% or stronger. For eye-washes  $\frac{1}{2}\%$  has been employed. It shrivels up soft corns, causing them to drop off if applied daily.

For a common cold, inhalation of 1% or equal parts of solution of formaldehyde and eau de Cologne is useful.

Ophthalmia, trachoma (1 in 2000 up to 1% used), and sweating feet are well treated by a lotion. Ringworm, lupus, laryngeal growths by pigment of 1 to 3 of glycerin. A spray or douche is useful for ozæna (1 in 2000 up to 1 in 500 with coarse spray).

Recurrent pleural effusion has been treated by intrapleural injection of glycerin 1 ounce, containing 10 drops of formalin.

Eczema in dry form should be treated with moist formalin application, e.g., 1 of formalin (40%) in a starch and water jelly 99. Weeping eczema may be treated with dusting powders containing formaldehyde.

Epithelioma on the face has been treated with formalin after using cocaine. The treatment is repeated after 4 days—the scab comes off and the surface below cicatrises rapidly. There is no local reaction, but the method is only suitable for epithelioma not larger than a florin. A solution of 2% formaldehyde is valuable in extensive and inoperable cases. It causes necrosis and elimination of neoplastic bodies without irritating healthy adjacent tissue or causing pain.

Aphthous ulcerations of the buccal mucous membrane may be washed with a tampon soaked in formalin. *Use cocaine first.*

Ringworm can be cured by painting with it, keeping the patch of skin in such a position that the solution will not run off it. One painting usually suffices. If skin greasy wash with spirit first. May smart a little but otherwise rapid, clean and effective. Second application may be repeated in 5 days' time.

For preserving and embalming animal tissues and museum specimens dilute about 10 times—for hardening about 25 times, but for preservative purposes a far weaker solution is sufficient.

For room disinfection and utensils 1 or 2% formalin as spray (coloured fabrics are not injured), or burn formalin disinfecting tablets, *q.v.* As a wash, up to 10% solution may be used. For furniture 1% would be suitable. Or simply *evaporate a pint of formalin per 1000 cu. ft. in an open vessel over a bunsen or spirit lamp.*

**Fumigators** are made for room disinfection. They are arranged to be lit at the bottom of the container whilst the fumigator stands on a tray with a little water. Formaldehyde is volatilised into the room and continues to be evolved for  $\frac{1}{2}$  hour. Windows, etc., to be pasted down in the usual way where complete disinfection is required, and clothing, etc., left exposed to the vapour for 3 or 4 hours.

**Formalin Disinfecting Tablets** are prepared from para-formaldehyde (*vide infra*) for use in a vaporiser or with a night-light—20 to 25 tablets per 1000 cubic feet, the latter number ensuring thorough disinfection. Walls and furniture should first be sprayed with water.

They are also prepared of strength 0.1, 0.25 and 0.5 g.

**TERMINAL DISINFECTION** during common epidemics "a procedure erroneously founded, almost always useless, and whose practical results bear no adequate relation to the labour and cost involved." Fumigation described by Dr. Andrew Balfour as "undoubtedly a process of camouflage." "Current" disinfection, *i.e.*, sterilisation of articles soiled by patient's excreta, and prompt disposal of excreta themselves, of more value—Prof. Chagas, *Lancet*, i/1928, 922

**Collutorium Formaldehydi (R.D.H.).** Solution of formaldehyde 18 m, oil of peppermint 5 m, alcohol (90%) 90 m, peppermint water to 1 oz. Use half a teaspoonful to a tumblerful of water.

**Garg. Antiseptic. (N.I.F.).** Solution of formaldehyde 16 m, boric acid 100 gr, glycerin 80 m, water to 8 oz. To be diluted with three parts of cold water.

**Gargarisma Formaldehydi (B.P.C.).** Solution of formaldehyde 0.2% *v/v*

[P2] **Liquor Formaldehydi Saponatus (B.P.C.)** contains 20% *w/v* of formaldehyde solution.

[P2] **Formalinsäpa, Terpiniform (P. Svec. X)**

Terpineol 5, alcohol (90%) 20, soft soap 40, formaldehyde solution 35. A pleasant, fragrant antiseptic preparation.

[P2] **Morestin's Fluid.**

**Dose.**—1 to 4 ml. injected drop by drop into the not completely evacuated sac.

A mixture of formalin, glycerin and alcohol equal parts.

In the treatment of hydrocele it is generally not painful. After a few hours the scrotum swells, becomes heavy and œdematous and some liquid reforms, but this is reabsorbed. Iodine has been used in children (congenital hydrocele), but is dangerous.—St. George B. Delisle Gray, *Brit. med. J.*, i/1930, 649, 726 (correction).

**[P1] Nebula Formaldehydi. C. MUTHU'S INHALANTS.**

**Inhalant "A."**—Chloroform 1 dr., menthol 10 gr., pumilio pine oil 10 m., alcohol (90%) to 1 oz., with 2½% of formaldehyde (in the form of gas). **"B."**—Guaiacol 1 dr., chloroform 1 dr., menthol 15 gr., pumilio pine oil 15 m., alcohol (90%) to 1 oz. with 5% formaldehyde. **"C."**—Guaiacol 2 dr., chloroform 2 dr., menthol 15 gr., pumilio pine oil 15 m., terebene 1 dr., alcohol (90%) to 1 oz. **"D."**—Guaiacol 2 dr., iodine 1 dr., terebene 1 dr., pumilio pine oil 15 m., chloroform 2 dr., alcohol to 1 oz.

**Dose.**—About 10 drops of one of the above sprinkled on the inhaler every ½ to 1 hour, and used by continuous inhalation.

These inhalations are used progressively. After reaching "C," "D" is used as an alternate solution or for night use.

About 50% of phthisical patients treated are stated to have recovered under the treatment.

**[P1] Formalin and Chloroform Solutions:—**

No. 1 Formalin 5, chloroform 15, alcohol (90%) 80.

No. 2 Formalin 10, chloroform 20, alcohol (90%) 70.

No. 2 is only ventured upon where formalin is well and easily endured. In the absence of the anæsthetic effect of the chloroform patients were not able to bear even the mild preparation for any length of time. Has given good results in phthisis.

**[P2] Cromessol** (*Cromessol Co, Glasgow*). An antiseptic containing formalin and essential oils

**Euguform** (*Chemische Fabrik Gustrow, Gustrow i. Meckl.; Braun, London*). Partially acetylated condensation product of guaiacol and formaldehyde. A dusting powder for wounds; antiseptic and analgesic

**Formadermine** (*Pharmaceutical Specialties (May & Baker) Ltd., London*). Methylenediguaiacol (a condensation product of guaiacol and formaldehyde). Supplied in the form of powder as an antiseptic and deodorant for indolent ulcers, burns, skin affections, etc. Also as a 5% toilet powder for superficial conditions

**Formosyl** (*Martindale, London*). A liquid formaldehyde potash soap. It is highly antiseptic, relatively non-poisonous, and miscible with water and alcohol in all proportions. Action of soap with the antiseptic power of formalin. A 2% solution is sufficient for general purposes and is better freshly prepared. For hand disinfection 1 to 2% is suitable. The stock bottles should be kept well corked. Available also as flavoured mouth-wash, gargle, tooth paste, etc.

**Yadil** (*Yadil, London*) is described as tri-methanal-allyl carbide. A water-white liquid having a slight allyl odour and a sweetish and pungent taste like formalin. Used as deodoriser and bactericide locally. For external use employ 1 in 300 as nasal spray, gargle or wash for offensive perspiration. Has been used for impetigo, acne, erysipelas, eczema and chilblains. For enemas and vaginal douches 1 in 150. For instruments 1 in 80.

Sir W. J. Pope found about 1% of formaldehyde, 4% of glycerin, with a minute quantity of either garlic or mustard oil. Prof. Dixon made indictments regarding its advertisement for cure of phthisis.—*Daily Mail*, July 22 and 23, 1924. It is very weak relatively to carbolic acid.—*J. Eyre, ibid.*, July 26, 1924.

**Paraformaldehydum (B.P.C.). Syn. PARAFORM, PARAFORMIC ALDEHYDE, TRI-OXY-METHYLENE (Fr. Cx.), FORMALDEHYDUM POLYMERISATUM (P. Belg. IV, U.S.P. XI, F.E. VIII) (H·COH), = 90·05.**

A white amorphous powder or friable mass, odourless at ordinary temperatures, but having a pungent odour when warmed, owing to evolution of formaldehyde. Is prepared by evaporating aqueous



formaldehyde solution; the polymer  $(\text{H COH})_n$  throws out, and on drying changes to paraformaldehyde

Catheters may be maintained aseptic by wrapping in lint impregnated with 20% of paraformaldehyde.

**Paraform Collodion**, 25% strength, applied 3 times a day to warts is efficacious

**DENTAL USE.** Paraformaldehyde, for the induction of painless dentine drilling, is mixed with Harvard Cement in the proportion of 1 to 20, and then made into a fairly firm mass with the fluid. If left in the cavity from 1-3 months, the cavity may be shaped without any pain to the patient. In addition, the slow emanation of formaldehyde gas over a lengthy period most probably arrests the process of decay. The cement should not be placed closer than half way to the nearest point of the pulp.—E. Clayton, *Trans Brit Soc Dent Surg*, 1925, 1, 33

**Pasta Formaldehydi (RDH)** Powder thymol 1 dr, and add paraform 3 gr, glycerin 10 m, zinc oxide 2 dr

**Tabellæ Formaldehydi (BPC)** *Syn* FORMALDEHYDE AND MENTHOL TABLETS, FORMAMINT TABLETS

*Note* The general use of the names "Formalin" and "Formamint" for tablets of formaldehyde is limited to Gt Britain and Northern Ireland

*Dose*—1 or 2 tablets. Contain about  $\frac{1}{2}$  gr of paraformaldehyde and  $\frac{1}{8}$  gr of menthol

**Formaldigen** (*Hewlett, London*) Brand of formaldehyde lozenges

**Formitrol Pastilles** (*Wander, London*) Brand of formaldehyde pastilles

**Aldehydum.**  $\text{CH}_2\text{COH}$  44.03 *Syn* ALDEHYDUM ABSOLUTUM, ALDEHYDE

A colourless mobile liquid, irritating when inhaled. Sp gr 0.80, b.p. 21. Becomes acid on keeping exposed to air—oxidation to acetic acid. Polymerises with rapidity in presence of sulphuric acid at atmospheric temperature into paraldehyde (*vide infra*), but if temperature be below 0° crystalline metaldehyde is formed

**Aldehydum Dilutum**

Contains 15%  $\frac{1}{2}$  in alcohol, is neutral to test paper, and has an ethereal suffocating odour, producing spasm of the glottis when respired. Diluted 1 in 1000 with water at 140 F has been used as inhalation in catarrh and ozema

**Paraldehydum** (B.P., U.S.P. XI, P. Ital. V, F.E. VIII, P. Helv. V)  $(\text{CH}_3\text{COH})_3 = 132.1$ .

*Dose*.—30 to 120 minims (2 to 8 ml), or more, in diluted syrup or almond mixture, repeated if needed in  $\frac{1}{2}$  an hour. U.S.P. XI average dose 30 minims

A colourless liquid, crystallising below 11°, sp gr 0.998. May be obtained by treating aldehyde with sulphuric acid

It has been stated (R. Hutchison, *Brit med J*, 1, 1930, 718) that paraldehyde may be oxidised by atmospheric oxygen, forming glacial acetic acid, but this does not occur under normal conditions of storage.

**Soluble** 1 in 10 of water, and miscible with alcohol, ether, chloroform and oils

If prescribed in greater proportion than will form a solution, it may be suspended with Pulv. Tragacanth. Co.

**Antidotes.** Empty stomach by emetic or stomach tube. Keep patient warm and awake, but do not walk him about. Ammonia inhalations. Strong coffee, with 5% dextrose, by rectum. Strychnine,  $\frac{1}{2}$  gr., hypodermically. Oxygen, or oxygen with 7% carbon dioxide, and artificial respiration if necessary.

Recovery after taking 2 oz of paraldehyde Stomach washed out with weak sodium bicarbonate solution, strychnine, Coramine and pituitrin administered, 1 pint of saline given intravenously, oxygen with carbon dioxide inhalations, 3 oz of black coffee by rectum —W More, *Brit med J*, 1/1934, 428

#### PARALDEHYDE HABIT

18 cases observed in 8 years Addicts not deterred by nasty taste If a nightly dose of 2 dr is continued for several weeks there is loss of appetite, gastro-intestinal irritation and flatulence, the patient becomes irritable, morose and suspicious, and may be mentally confused and agitated, with muscular weakness and tremor of hands Tolerance is established and increased dose demanded (max single dose of 3 ounce often known to be exceeded) The final picture is one of mental and physical deterioration Paraldehydism always superimposed on other forms of addiction, most commonly alcoholism Alcohol and paraldehyde tend to reinforce one another in action —A E Carver, per *Lancet*, 1/1934, 408

**Uses.** As a sedative and hypnotic, but without action on the heart In spasmodic asthma it relieves spasm and induces sleep In delirium tremens 100 minims is a safe hypnotic

*Per rectum* it is an anæsthetic and hypnotic, *v. postea*.

It is diuretic It sometimes produces rash and digestive disturbances, and slight excitement

**RECTAL ANÆSTHESIA** Paraldehyde 9 dr—the customary drachm per stone weight—in 5 oz of olive oil, for dental operation Error in copying by a third party, stating 9 oz, caused death —*Lancet*, 1/1929, 247

Before operations paraldehyde (*per rectum*) not very successful —H R Phillips, *Brit. med J*, 1/1930, 279

Paraldehyde before and after anaesthesia —R Francis Matters, *Brit med J*, 1/1930, 1112

Rectal paraldehyde as preliminary to tonsillectomy in children is of value 1 dr in 14 oz of saline, neither warmed nor cooled, per stone weight, an hour before operation —M Sourasky, *Brit med J*, 1/1930, 993

Valuable as a basal hypnotic *per rectum*, 1 dr per stone, given slowly 1½ hours before operation in 10 times its quantity of normal saline Atropine as usual, and morphine to adults Specially useful for children —I W Magill, *Lancet*, 1/1931, 353 Easy to work with on the upper air passages —C H Thomas, *ibid.*, 354

In the treatment of the *status epilepticus*, paraldehyde by rectum in a dose of 6 dr, the dose to be repeated if necessary, is a valuable remedy —E Bramwell, *Practitioner*, 11/1933, 333

The evening before operation give an enema or a sedative The following morning, 1½ hours before operation, give 100 gr of atropine hypodermically and immediately afterwards 8 dr of paraldehyde (less if patient under 8 stone) in 12 oz of saline, freshly mixed and thoroughly shaken The paraldehyde must be fresh The patient remains comfortable for 24 hours following operation, and distressing recollections are absent —J. Duke Stewart, *Brit med J*, 11/1932, 1139

Administration *per rectum* as a preliminary to general anaesthesia in 200 consecutive cases Procedure described —J. R. M Whigham, *Lancet*, 11/1934, 191

While there can be no doubt that in some selected cases the use of paraldehyde, given in oil *per rectum* during the first stage of labour, may be a valuable means of relieving pain, the general opinion of those who have used it as a routine method in this investigation is that it is unsuitable for general use by midwives —Report of an Investigation by the College of Obstetricians and Gynaecologists at the request of the National Birthday Trust Fund, per *Lancet*, 1/1936, 283

#### Elixir Paraldehydi.

Dose —1 to 3 drachms (4 to 12 ml.).

Paraldehyde 240, glycerin 240, alcohol (90%) 480, oil of cinnamon 4, oil of bitter orange 8, saccharin 1.

**Enema Paraldehydi (B.P.C.).**

*Dose.*—1 drachm (4 ml.) per stone body weight with 5% w/v dextrose in normal saline.

**Mistura Paraldehydi.**

Paraldehyde 2 dr., essential oil of almond (s.A.P.) 3 m, syrup 1 oz., liquid extract of liquorice 2 dr., water to 4 oz. This covers the nauseous taste to some extent and forms four doses of  $\frac{1}{2}$  drachm or two doses of 1 drachm.

**Mistura Paraldehydi et Potassii Iodidi.**

*Dose.*—1 drachm (4 ml.).

Paraldehyde 1 25, potassium iodide 0 92, liquid extract of liquorice 6 25, water to 100

In broncho-pneumonia and capillary bronchitis of infants it is valuable. The constituents of the mixture are incompatible, free iodine being formed but not sufficient to harm. In severe cases the secretions dry up remarkably.

**Metaldehyde** ( $C_2H_4O$ )<sub>3</sub>. A polymer of acetaldehyde occurring as a white crystalline solid, burning readily and subliming at 100°.

**Meta** (*Elmesan, London*). Compressed metaldehyde for use as a solid fuel, burning with a non-luminous carbon-free flame.

Poisoning in a boy of 16 through taking 5 g of metaldehyde. Treatment consisted in giving large doses of alkalis and controlling the convulsions with chloral hydrate and potassium bromide—*Lancet*, 11/1927, 670

Two cases of poisoning in children after eating the tablets in mistake for sweets—acute poisoning of the central nervous system. Treatment gastric lavage and purge—*Brit med J*, 1/1929, 120

Death of a young woman student after eating nearly an ounce—*Lancet*, 11/1933, 194.

Poisoning in a child of 20 months—recovery—A French, *Brit. med. J*, 11/1935, 974.

**Meta Poisoning Treatment.**

(1) Immediate wash-outs of stomach with large quantities of sodium bicarbonate solution; repeat frequently and perform slowly for first time, (2) high colon wash-outs of bowels with alkaline solutions, (3) purgatives after washing-out—Glauber's salts or castor oil, (4) large quantities of charcoal (preferably wood), (5) caffeine, and, if necessary, strophanthin intravenously, (6) no narcotics if possible—sodium barbitone if cramps intensive, (7) Calcium-Sandoz intravenously and 30 to 40% dextrose repeatedly intravenously.—*Elmesan Ltd, Brit med. J.*, 1/1934, 132

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**GELATINUM**

*B.P., U.S.P. XI, P. Dan.*

Nearly colourless transparent sheets or shreds made by extracting animal tissues, bones, etc., with boiling water.

**Skin Gelatin** is the best. It is more pliable, possesses more "fibre," and is suitable for gelatin capsule-making. Bone gelatins made from osseine (acidulated bone) are brittle and hence

unsuited. *U.S.P. XI* requires gelatin for capsule-making to contain not more than 0.15% of  $\text{SO}_2$ .

*Dose.*—*Ad libitum per os*, and injected

*Uses.* Gelatin taken *per os* is easy of digestion, the cleavage products being largely absorbed. It is first converted by pepsin into proteoses and peptones. Trypsin of the pancreatic juice then splits these into amino-acids. Hypodermically the 1 to 2% solution has been used to check bleeding from the lungs and kidneys and to relieve aortic aneurism. 100 ml. or more of 2% solution may be injected into the gluteal region. These injections may be followed by pain, fever, local swellings and nettle rash. Other hæmostatics may be combined with it. It has been given orally to arrest hæmorrhage of the stomach in ulcer and cancer, and of the intestines in typhoid and dysentery. Oozing hæmorrhage from mucous surfaces due to snake bite is also well treated by large quantities given orally. Solutions of gelatin for injection must be sterilised with great care, since tetanus spores are liable to be present.

For visceral pains and for speeding up healing process 5 or 10 ml. of 5% solution injected. Aneurism (60 cases) well treated with 100 ml of 2% solution weekly.—*Per J Amer med Ass*, 1/1926, 519

**Gelatina Soluta Sterilisata** (*P. Helv V*) is approx 9% in normal saline. The warm solution is nixed with the white of an egg, heated in an autoclave until a temperature of  $120^\circ$  is reached (should not occupy more than 30 minutes), then allowed to cool to normal pressure and filtered. It is distributed into sterile tubes which are sealed and steamed for half an hour on three consecutive days. The tubes are then incubated for a week at  $37^\circ$ , and any contaminated are rejected.

**Liquor Gelatinæ Sterilisatus** (*P. Jap IV*) is similar, but strength of sodium chloride is 0.5%

**Soluté de Gélatine Injectable** (*Fr. Cx Supp*, 1926)

Gelatin 10 g, sodium chloride 8 g, distilled water to 1000 ml. Neutralise to litmus accurately by adding drop by drop N/10 sodium hydroxide. Sterilise for 15 minutes at  $115^\circ$  in an autoclave

**GELATINOTHORAX.**

Treatment of empyema thoracis by intrapleural injection of 2% gelatin solution with antiseptics such as euflavine or acriflavine 1 in 2000

An initial injection of 5 or 10 ml only is given to test response. Should be tried before siphonage, suction drainage, or operation.—*J. Crockett, Brit. med. J.*, 1/1931, 684, *Lancet*, 1/1931, 758. See also R. A. Hunter, *Tubercle*, Feb., 1931.

**Sterules of Concentrated Gelatine Saline** (*Martindale, London*) contain 1 oz. of solution which when diluted to 10 oz. yields a 2% solution. A smaller size yields 2oz of 2% solution. Sterules of euflavine 1 gr are issued for use in conjunction with the gelatin solution

**Thoragel** (*Pharmaceutical Specialities (May & Baker) Ltd, London*) Solution for gelatinothorax containing 5% of gelatin and 1 in 2000 of acriflavine. **Thoragel "C"** has 2 or 5% of calcium chloride in addition. *Dose.*—In tuberculosis of lungs 5 to 15 ml. intrapleurally or up to 5 ml. intrapleurally; in tubercular glands in a state of flocculation withdraw 3 to 5 ml and inject 3 to 5 ml of the solutions. In tubercular laryngitis it may be used as spray for the throat

**Formalised Gelatin.** This has been used with success as a substitute for collodions. Gelatin solution 10% in water is stored in wide-mouth test-tubes holding 3 oz. each. The tubes are plugged with cotton wool and sterilised, at  $100^\circ$  for 15 minutes, on three successive days. When required for use, melt in a water-bath

and add 1 dr. of formalin solution diluted 10 times, *i.e.*, 4% strength of formaldehyde approx—the final product will then contain a little over 1% of formaldehyde, or fully 2½% of commercial formalin solution

The wound is dressed with a thick roll or pad of sterilised gauze, with a piece of stiff gauze above extending beyond the wound. The formalised gelatin is applied with a swab on the top of the stiff gauze beyond the limit of the wound—thus holds the dressing in place without bandage—Communicated by the Dispenser, General Infirmary, Leeds

**Glycogelatinum (B.P.C.)** A flavoured pastille basis containing 20% of gelatin.

**Glyco-gelatin (T.H.)** Gelatin 1 oz, glycerin 2½ oz (by weight), orange-flower water 2½ oz; soak the gelatin in the water, then heat until dissolved, add the glycerin and, when nearly cold, carmine solution *q s*. Is a softer basis than that of the *B.P.C.*

**Gelatinum Glycerinatum (U.S.P. XI)** Soak gelatin 1, for 1 hour, in boiled and cooled water to cover it. Drain and add glycerin 1 (by weight), heat to dissolve, strain and evaporate to 2

**Ichthyocolla (B.P.C., P. Belg. IV, F.E. VIII, P. Ital. V)** *Syn* ISINGLASS

The swimming bladder of certain species of the sturgeon and hake, dried and sliced into thin pieces. About 3 drachms to the pint of warm water forms a jelly. Is used for refining wine. Isinglass plasters on muslin or on silk (court plaster, *Emplastrum Adhæsivum Anglicum P. Jap. IV*) are prepared with a 1 in 6 or 1 in 8 solution

**Sinclair's Glue.** For applying extension in fractures instead of plaster. Melt on water-bath when required and apply with the hand, using a bandage if necessary

Very good glue or gelatin 50, water 100, glycerin 4 or 6, thymol or menthol 0.15%. The smaller amount of glycerin is for summer or tropical use and the larger amount for winter. The blistering occasionally reported is due to the excessive pull exerted by the gauze. If patient complains of a tickling or burning sensation, the dressing must be removed, or in any case every 10 to 14 days

When extra traction is needed, or for very tender skins, the following formula is occasionally used—Isinglass 50, gelatin 50, water 200, tannic acid 12, glycerin 8 or more, thymol or menthol 0.15%.

Previous formulæ containing calcium chloride are no longer used—W. A. Knight, *Pharm. J.*, 1/1935, 7.

**Pectin.** A complex carbohydrate contained in many fruits and vegetables. It has a sweetish, glutinous taste. It reduces Fehling's solution. When boiled with sugar in acid media it forms a jelly. Pectin is used extensively in the manufacture of jams and jellies

Pectin-sugar-acid gels can be obtained with 0.125% of pectin, but jams usually contain 0.5 to 1%. For 1% pectin the lower limit for sugar content is 50%, and the higher 75%. Less than 66% sugar grows moulds and yeasts. Gooseberry juice, apple and lemon are used commercially as additions where the fruit is not rich, *e.g.*, strawberry, cherry, raspberry, blackberry, rhubarb—S. Black, *Pharm. J.*, ii/1931, 44.

Pectin manufacture—*Pharm J*, 11/1929, 388

A powder consisting of pectin 10 g, tragacanth 12 g, acacia 16 g, gelatin 7.8 g is a good emulsifying agent. 18 g of the powder triturated with 100 g of water, allowed to stand for 30 minutes and then 400 g of boiling water gradually added will emulsify 400 g. of cod-liver oil, added in 5 separate portions with vigorous shaking.—W. Brandrup, per *Chem & Drugg*, 11/1934, 778

**Arhemapectyl** (*Gallier, Paris*) A colloidal isotonic solution of pectin and calcium for use in hæmorrhage. Is non-toxic by ingestion up to 80 ml. 1% solution, and has no contraindications. Supplied in ampoules and pessaries

## GELSEMIUM

B.P.C.

Syn GELSEMI RADIX

[P1] “Alkaloids, the following, their salts, simple or complex — *Gelsemium*, alkaloids of”

[81] “Alkaloids, the following, their salts, simple or complex — *Gelsemium*, alkaloids of, except substances containing less than 0.1% of the alkaloids of *gelsemium*”

[86] “Alkaloids—*Gelsemium*, alkaloids of—specify proportion as the proportion of any one alkaloid of *gelsemium* that the preparation would be calculated to contain on the assumption that all the alkaloids of *gelsemium* in the preparation were that alkaloid”

Dose —  $\frac{1}{4}$  to 1 grain (0.015 to 0.06 g.)

The dried rhizome and roots of “yellow jasmine,” *Gelsemium sempervirens* (Loganiaceæ), imported from the United States. Must be distinguished from the yellow jasmine cultivated here, which is a species of *Jasminum*. The drug contains the alkaloid gelsemine and an amorphous mixture of alkaloids called gelseminine. The latter has the greater physiological activity.

**Antidotes.** Empty stomach by emetic or by stomach tube, using dilute solution of tannic acid. Keep patient warm, give brandy,  $\frac{1}{2}$  oz., or aromatic spirit of ammonia,  $\frac{1}{2}$  dr., in water. Artificial respiration and oxygen with 7% carbon dioxide inhalations if necessary.

Accidental death from an overdose in the case of a woman suffering from neurasthenia. *Pharm J*, 1/1927, 558

**Uses.** Febrifuge, antispasmodic and analgesic. In acute and rheumatic neuralgia, toothache, uterine and ovarian pain and chorea. It is a powerful paralyzant and respiratory poison. Large doses contract the pupil and cause giddiness and diplopia.

[P1 81] **Extractum Gelsemii** (B.P.C.)

Dose —  $\frac{1}{2}$  to 2 grains (0.03 to 0.12 g.). A soft extract

[P1 81] **Extractum Gelsemii Liquidum.** By percolation with a mixture of alcohol 4 and water 1. Strength 1 = 1. Average dose —  $\frac{1}{2}$  minim

Dysmenorrhœa is well treated by 3 minim doses with 5 minims of tincture of belladonna thrice daily

For examination nervousness a small dose thrice daily is a tonic.

[P1] **Mistura Gelsemii** (R.L.O.H.) Sodium salicylate 10 gr., sodium bicarbonate 10 gr., potassium bromide 10 gr., tincture of gelsemium 10 m., chloroform water to 1 oz. For neuralgia and generally as a sedative.

**[P1 81] Tinctura Gelsemii (B.P.C.).**

*Dose.*—5 to 15 minims (0.3 to 1 ml.). 1 in 10.

*Uses.* For neuralgia of face and jaws associated with carious teeth—15 m. every 6 hours may give relief. Is often given with ammonium or potassium bromide. In rheumatoid arthritis it is given with *cinicifuga q.v.* Disordered vision may follow even moderate doses.

INFLUENZA well treated by the following.—Gelsemium tincture 12 m., belladonna tincture 5 m., potassium citrate 10 gr., syrup of orange 1 dr., chloroform water to 1 oz. *Dose*—1 ounce every 4 hours. Afterwards  $\frac{1}{2}$  oz. until temperature falls to normal. Headache and backache vanish, with general improvement. The only disadvantage is that gelsemium may cause ocular disturbance — W. D. D. Small and W. O. Blanchard, *Brit. med. J.*, 1/1919, 241

**[P1 81] Gelsemina (B.P.C.).**  $C_{20}H_{22}O_2N_2 = 322.2$ 

*Dose.*— $\frac{1}{15}$  to  $\frac{3}{80}$  grain (0.0005 to 0.002 g.) in pills

Minute white crystals, m.p.  $178^{\circ}$ , with a bitterish taste, sparingly soluble in water, easily in alcohol, ether and acids. It forms crystalline salts, and has mydriatic properties, but it is now used only for trigeminal neuralgia.

**P1-81] Gelseminæ Hydrochloridum.**  $C_{20}H_{22}O_2N_2.HCl = 358.7$ 

*Dose.*— $\frac{1}{15}$  to  $\frac{3}{80}$  grain (0.0005 to 0.002 g.).

In white, granular crystals, freely soluble in water

**GENTIANA**

(with CALUMBA, QUASSIA, etc.)

*B.P., U.S.P. XI, P. Helv. V, P. Dan.*

*Syn. RYUTAN (P. Jap. IV).*

*Dose.*—10 to 30 grains (0.6 to 2 g.).

The dried rhizome and roots of *Gentiana lutea* (Gentianaceæ).  
A bitter tonic.

**Extractum Gentianæ (B.P.)**

*Dose.*—2 to 8 grains (0.12 to 0.5 g.). A soft aqueous extract used as a pill excipient.

**Infusum Gentianæ Compositum Concentratum (B.P.)**

*Dose.*— $\frac{1}{2}$  to 1 drachm (2 to 4 ml.).

Gentian about 1 in 10 with dried bitter orange peel and lemon peel in alcohol 25%.

**Infusum Gentianæ Compositum Recens (B.P.).**

*Dose.*— $\frac{1}{2}$  to 1 ounce (15 to 30 ml.).

Gentian 1 in 80 with dried bitter orange peel and lemon peel.

**Mistura Gentianæ Acida (B.P.C.).**

*Dose.*— $\frac{1}{2}$  to 1 ounce (15 to 30 ml.).

Contains 12 m. of dilute nitro-hydrochloric acid with syrup of orange, compound infusion of gentian and chloroform water to 1 oz.

**Mistura Gentianæ Alkalina (B.P.C.).** *Syn.* MISTURA GENTIANÆ CUM SODA.

*Dose.*— $\frac{1}{2}$  to 1 ounce (15 to 30 ml.).

Contains 15 gr. of sodium bicarbonate and 5 gr. of ammonium carbonate with syrup of orange and compound infusion of gentian 1 oz.

**Pastilli Stomachici (P. Jap. IV)** Sodium bicarbonate 0.25 g., gentian 1 g.

**Tinctura Amara (P.G. VI).** Gentian 3, centaury root 3, orange peel 2, orange berries 1, zedoary root 1, diluted alcohol (67 to 69% v/v) to 50.

**Tinctura Gentianæ Composita (B.P.)**

*Dose.*— $\frac{1}{2}$  to 1 drachm (2 to 4 ml.). Gentian 1 in 10 with dried bitter orange peel and cardamom in alcohol 45%

**Tinctura Gentianæ Composita (U.S.P. XI).**

*Average dose.*—60 minims (4 ml.).

Similar in composition to Tinct. Gent. Co. B.P., but contains also about 10% of glycerin.

**Azadirachta.** *Syn.* NIM or NEEM, MARGOSA. The bark of *Melia Azadirachta* (Meliaceæ), indigenous to India. Used as a bitter instead of gentian or quassia.

In tropical granulomata sodium and potassium salts of margosic acid (from oil of margosa seeds) in 2 to 3 grain doses in 4% solutions intramuscularly have been tried, but caused irritation. Intravenously, blocking of the veins occurred. Ethyl margosate as a further step has been employed, it is non-irritant and has antiparasitic and bactericidal properties.—K. K. Chatterji, *Lancet*, ii/1925, 1063

**Calamus (B.P.C.).** *Syn.* SWEET FLAG ROOT. *Dose.*— $\frac{1}{2}$  to 1 drachm (1 to 2 g.) The dried rhizome of *Acorus Calamus* (Araceæ). Aromatic bitter and aromatic **Tinctura Calami.** *Dose.*— $\frac{1}{2}$  to 1 drachm. 1 in 5. **Infusum Calami.** *Dose.*— $\frac{1}{2}$  to 1 ounce. 1 in 10

**Calumba (B.P., P. Helv. V, P. Dan.).** *Syn.* RADIX FRASERI. The dried root, sliced, of *Jateorhiza palmata* (Menispermaceæ).

Bitter tonic for simple debility and indigestion. Contains no anin and can be given with salts of iron

False calumba root is from *Coscinum fenestratum*.

**Infusum Calumbæ Concentratum (B.P.)** *Dose.*— $\frac{1}{2}$  to 1 drachm (2 to 4 ml.) About 1 in 2 $\frac{1}{2}$ .

**Infusum Calumbæ Recens (B.P.)** *Dose.*— $\frac{1}{2}$  to 1 ounce (15 to 30 ml.). 1 in 20.

**Tinctura Calumbæ (B.P.).** *Dose.*— $\frac{1}{2}$  to 1 drachm (2 to 4 ml.).

1 in 10 of alcohol 60%.

**Cascarilla (B.P.C., P. Dan.).** The dried bark of *Croton Eluteria* (Euphorbiaceæ). Contains 1.5 to 2% of volatile oil, also the bitter principle cascarillin. Aromatic tonic.

**Infusum Cascarillæ Concentratum (B.P.C.).** *Dose.*— $\frac{1}{2}$  to 1 drachm (2 to 4 ml.). About 1 in 2 $\frac{1}{2}$

**Infusum Cascarillæ Recens (B.P.C.).** *Dose.*— $\frac{1}{2}$  to 1 ounce (15 to 30 ml.). 1 in 20.

**[P.] Mistura Cascarillæ Composita (St. T.H.).** Camphorated tincture of opium 15 m., vinegar of squill 20 m., emulsion of chloroform 10 m., infusion of cascarilla to 1 oz.

**Tinctura Cascarillæ (B.P.C.).** *Dose.*— $\frac{1}{2}$  to 1 drachm (2 to 4 ml.). 1 in 5.

**Chirata (B.P.C.).** The dried plant, *Swerteria Chirata* (Gentianaceæ).



*Dose* —5 to 30 grains (0·3 to 2 g.).

A bitter tonic given in indigestion for anorexia and torpid liver with constipation

**Infusum Chiratae Recens** (*B P C*) *Dose* — $\frac{1}{2}$  to 1 ounce (15 to 30 ml.) 1 in 20.

**Infusum Chiratae Concentratum** (*B P C*) *Dose* — $\frac{1}{2}$  to 1 drachm (2 to 4 ml) 1 in  $2\frac{1}{2}$

**Tinctura Chiratae** (*B P C*)

*Dose* — $\frac{1}{2}$  to 1 drachm (2 to 4 ml) 1 in 10

**Cimicifuga** (*B P C*). *Syn.* BLACK SNAKEROOT, BLACK COHOSH, ACTÆÆ RACEMOSÆ RADIX.

*Dose* —8 to 15 grains (0·5 to 1 g.).

The dried rhizome and roots of *Cimicifuga racemosa* (*Ranunculaceæ*).

**Extractum Cimicifugæ Liquidum** (*B P '98*) *Dose* —5 to 30 minims (0·3 to 2 ml) 1 in 1

**Tinctura Cimicifugæ** (*B P C*). *Syn.* TINCTURA ACTÆÆ RACEMOSÆ

*Dose* — $\frac{1}{2}$  to 1 drachm (2 to 4 ml) 1 in 10

In rheumatoid arthritis 15 minims of tincture with 5 minims of tincture of gelsemium thrice a day is often useful

**Cimicifugin.** *Dose* —1 to 6 grains in pill Is the resinous body obtained by pouring a strong tincture into water Useful in chronic rheumatism, lumbago, sciatica, chorea, and amenorrhœa

**Otosclerol** (*Coates & Cooper, London*) A preparation containing cimicifugin, bromides, and combined phosphorus For deafness *Dose* —1 tablet thrice daily after meals, increased if necessary

**Condurango** (*B P C, P G VI, P Ital V, P Belg IV, P Helv V, P. Dan.*)

*Dose* — $\frac{1}{4}$  to 1 drachm (1 to 4 g) in powder

The stem bark of *Marsdenia Condurango* (*Asclepiadaceæ*) from Ecuador Is bitter and acrid A stomachic and stimulant in dyspepsia

**Extractum Condurango Liquidum** (*P G VI*) is made 1 in 1 with alcohol 1 and water 3

**Vinum Condurango** (*P G. VI*) *Dose* — $\frac{1}{4}$  to 1 ounce (15 to 30 ml) Liquid extract 10, aromatic tincture 1, sucrose 9, sherry 80 (*Tinctura Aromatica* (*P G VI*) is cinnamon 5, ginger 2, galanga 1, clove 1, cardamom 1, alcohol 69% v/v 50)

**Galanga** (*B.P.C, P Helv V, P Dan*) *Syn.* LESSER GAI AN-GAL, EAST INDIAN ROOT, CHINA ROOT

*Dose.* — $\frac{1}{4}$  to  $\frac{1}{2}$  drachm (1 to 2 g.)

The dried rhizome of *Alpinia officinarum* (*Zingiberaceæ*) Aromatic and carminative. Has been used as decoction (1 in 20).

**Inula.** *Syn.* ELECAMpane. The dried rhizome and roots of *Inula Helenum* (*Compositæ*). Antiseptic, given internally in bronchitis as **Extractum Inulæ Liquidum**, 1 = 1, *dose* —10 to 60 minims.

**Lupulus** (*B.P.C*). *Syn.* HOPS, HUMULUS, STROBILI LUPULI. The dried strobiles of the hop plant, *Humulus Lupulus* (*Cannabaceæ*). An aromatic bitter, formerly believed to possess sedative properties. The use of pillows stuffed with hops is reputed to induce sleep.

**Extractum Lupuli (B.P.C.).**

*Dose*—5 to 15 grains (0.3 to 1 g.) A soft extract. A liquid extract, 1 in 1, *dose*—5 to 15 minims, is also available.

**Infusum Lupuli Concentratum (B.P.C.)**

*Dose*—1 to 2 drachms (4 to 8 ml.)

About 1 in 2½. This preparation diluted with 7 volumes of water may be dispensed when Infusum Lupuli is prescribed.

**Tinctura Lupuli (B.P.C.).**

*Dose*—½ to 1 drachm (2 to 4 ml.) 1 in 5

**Lupulinum (B.P.C., P. Helv. V)**

*Dose*—2 to 5 grains (0.12 to 0.3 g.) in pills, capsules or cachets.

A yellow powder, becoming brownish with age, consisting of the glandular trichomes from the strobiles of the hop plant.

**Menyanthes Trifoliata (P. Dan.)** *Syn.* TRIFOLIA FIBRINA, BOGBEAN LEAF, HUCKLEBERRY. Bitter tonic, emmenagogue, antiscorbutic, vermifuge and febrifuge. Large doses are purgative and emetic, contains menyanthin, a glucoside. Infusion 1 in 20. *Dose*—2 to 6 ounces, taken hot, early in the morning daily, useful for functional amenorrhœa. Liquid extract with liquorice 1 in 2. *Dose*—½ ounce.

**Quassia (B.P., P. Helv. V) *Syn.* JAMAICA QUASSIA.**

*Dose*—2 to 8 grains (0.12 to 0.5 g.)

Stem-wood of *Picræna excelsa* (Simarubaceæ). Contains picrosamin. Is chiefly employed as a bitter tonic. Is free from tannin, hence compatible with iron preparations. *Surinam Quassia* (not now in use) is the wood of *Q. amara*, a branching shrub, whereas *P. excelsa* is about 100 feet high.

A strong infusion, administered by rectal injection, will remove tape-worms and thread-worms. The latter have been discharged on the third day by 2-grain quassia extract pills (keratin coated)—one morning, noon and night. Previously 2 ounces of compound decoction of aloë.

**Quassia Suppositories** containing ½ grain of extract with gelatin basis (15 minim size) are prepared. These have been found valuable for removal of thread-worms in young children. They are simple and convenient to use in comparison with enemata. The strength may be increased.

**Anti-smoking Gum.** Quassia made up in form of a chewing gum has been used as a substitute for smoking for the use of patients suffering from tobacco amblyopia who feel the loss of their tobacco. If alcoholic complication is absent 1 in 20 is strong enough.

**Enema Quassiæ (B.P.C.)**

*Dose*—20 ounces (600 ml.) of the fresh infusion.

**Extractum Quassiæ (B.P.C.).**

*Dose*—3 to 5 grains (0.2 to 0.3 g.). A soft extract.

**Infusum Quassiæ Concentratum (B.P.).**

*Dose*—½ to 1 drachm (2 to 4 ml.) 1 in 12½, extracted with cold water, and alcohol added.

**Infusum Quassiæ Recens (B.P.).**

*Dose*—½ to 1 ounce (15 to 30 ml.) 1%. Prepared with cold water.

[P2] **Lotio Quassiæ.** Concentrated quassia infusion 1 oz., spirit of rosemary 1½ dr., sassafras oil 30 m., alcohol 2 dr., liquefied phenol 2 dr., water to 6 oz. Shake before use. For nits in children's hair.

**Tinctura Quassiae (B.P.).** *Dose.*— $\frac{1}{2}$  to 1 drachm (2 to 4 ml.). 1% in alcohol 45%.

**Quassinum.** *Syn.* PICRASMIN. A dry alcoholic extract in white odourless intensely bitter crystals. *Fr. Cx.* gives max. single dose, and *F.E. VIII* average dose,  $\frac{1}{8}$  grain.

[P1-81] **Quebracha (B.P.C.).** *Syn.* QUEBRACHO, ASPIDOSPERMA, QUEBRACHO-BLANCO.

[P1] "*Alkaloids, the following; their salts, simple or complex:—Quebracho, alkaloids of, other than the alkaloids of red quebracho*"

[81] "*Alkaloids, the following; their salts, simple or complex:—Quebracho, alkaloids of.*"

[88] "*Alkaloids—Quebracho, alkaloids of, other than the alkaloids of red quebracho—specify proportion as the proportion of any one alkaloid of quebracho that the preparation would be calculated to contain on the assumption that all the alkaloids of quebracho in the preparation were that alkaloid*"

The dried bark of *Aspidosperma Quebracho* from Argentina Tonic, febrifuge and antispasmodic. [P1 81] Tincture of quebracho, 1 in 5, of alcohol 60%, *dose.*—1 drachm [P1 81] Liquid extract, 1 = 1, *dose.*—10 minims.

Red quebracho bark is recognised as distinct in the Index Kewensis. It is used in making tannin extract.—E. M. Holmes, *Pharm. J.*, 1/1926, 4, II/1929, 194

**Serpentaria (B.P., U.S.P. XI).**

*Dose.*— $\frac{1}{4}$  to 1  $\frac{1}{2}$  grains (0.05 to 0.1 g.) U.S.P. XI average dose 15 grains.

The dried rhizome and roots of *Aristolochia reticulata* (Texan Serpentry) (Aristolochiaceæ) A bitter tonic.

**Infusum Serpentariæ Concentratum (B.P.C.)**

*Dose.*— $\frac{1}{4}$  to 1 drachm (2 to 4 ml.)

1 in 2  $\frac{1}{2}$ . When Infusum Serpentariæ is prescribed this preparation diluted with 7 times its volume of water may be dispensed

**Tinctura Serpentariæ (B.P.C.).** *Dose.*— $\frac{1}{4}$  to 1 drachm (2 to 4 ml.) 1 in 5

**Aristolochia (B.P.C.).** *Syn.* INDIAN BIRTHWORT, SAPSUN. The dried stem and root of *Aristolochia indica* (Aristolochiaceæ) A bitter used in the East for the same purpose as serpentary. Is administered as **Tinctura Aristolochiæ**, 1 in 5, *dose.*— $\frac{1}{4}$  to 1 drachm

## GLYCERINUM

*B.P., U.S.P. XI.*

$\text{CH}_2\text{OH} \cdot \text{CHOH} \cdot \text{CH}_2\text{OH} = 92.06.$

*Dose.*—1 to 2 drachms (4 to 8 ml.); by rectal injection,  $\frac{1}{2}$  to 2 drachms (2 to 8 ml.). U.S.P. XI average dose 60 minims.

*Intravenously*, 1 drachm (4 ml.) has been given with equal amount of tap water (*v. postea*).

**Manufactured** by decomposing fats with alkali or superheated steam. Sp. gr. 1.260 to 1.265. **Miscible** with water and alcohol 90%; but immiscible with ether or chloroform.

*P. Ned.* *V* permits 11·7 to 13·6% of water (sp. gr. 1·230 to 1·235). *P. Dan.* 12 to 15% (sp. gr. 1·225 to 1·235); *P. Helv.* *V* 12 to 16%. The latter includes also Glycerinum concentratum containing at least 98% of  $C_3H_8O_3$ . *U.S.P. XI* requires not less than 95%.

CRYSTALLISATION of glycerin occurs occasionally in the cold weather. The crystals do not melt again until temperature is about 20°.

**Uses.** Internally tends to relax the bowels. Is added to cough mixtures and to relieve forms of indigestion with gaseous distension. As an enema,  $\frac{1}{2}$  ounce alone or with  $\frac{1}{2}$  water added relieves constipation and reduces piles. Externally, 1 with 2 or 3 of water prevents cracks of chilblains, and forms an ingredient in a large number of skin applications. It is a useful solvent for many active principles of drugs, standing midway between alcohol and water, cf. Glycetracta. It is also a valuable preservative, cf. "Aqueous" Tinctures.

#### Germicidal Action of Glycerin.

In strong concentrations in culture media glycerin acts as a deterrent to growth, the inhibition being of a hindering nature rather than bactericidal. Organisms possess different degrees of resistance to contact with glycerin, the gonococcus and streptococcus being the most fragile. Vastly superior to potassium permanganate for antiseptic and surgical use when dealing with an organism like the staphylococcus. Valuable results by intrauterine injections in septic conditions of the uterus and its appendages—A. Compton, *Lancet*, 11/1926, 326 (*v postea*).

Glycerin when diluted to about 50% is an efficient germicide and rendered possible the introduction of glycerinated lymph. It kills staphylococci, streptococci, and the bacilli of tubercle, diphtheria and enteric. The only organisms resistant to 40% glycerin longer than a month are spores of the hay bacillus, spores of *B. mesentericus vulgatus*, the common pink yeast, and *B. coli*, when kept in the cold—S. Monckton Copeman, *Brit. med. J.*, 1/1931, 513.

BOILS AND CARBUNCLES, and all kinds of wounds and sores, effectually treated covered by gutta-percha tissue or oiled cambric. Also good in eczema. Absence of bleaching and maceration of the skin—D. Kyle, *Brit. med. J.*, 1/1931, 76.

CANCER—Metabolism of tumours. J. T. Shirlaw states that cancer frequently develops in people who have previously suffered from glycosuria of the non-pancreatic type. The only explanation for the non-combustion of the sugar is that the fatty acids are not sufficiently unsaturated by the liver ferments and lipase. Combustion of fats and carbohydrate is therefore incomplete, causing superabundance of fatty acids with possible formation of saponins, which are extremely irritating, and the alteration of surface tension produced has a profound influence on the division of cells. Glycerin injected intravenously (1 drachm in 1 drachm of boiled tap water) thought to combine with fatty acids and form innocuous fat. A case of scirrhus of the breast so treated showed considerable improvement. Small quantities of tin also act as catalyst and assist synthesis of glycerin and fatty acids into fat, and 2 ml. Stannoxyl intramuscularly were given simultaneously with the glycerin injection.—*Brit. med. J.*, 1/1931, 74.

CELLULITIS. Glycerin in combination with Liq. Hyd. Perchlor. excellent for all kinds—H. A. Morton-Whitby, *Brit. med. J.*, 1/1931, 206.

TUBERCULOUS PERITONITIS treated by glycerin 1 pint intraperitoneally—in desperate cases beneficial but toxic—A. MacLennan. Probably diluted just as good—D. Kyle, *Brit. med. J.*, 1/1931, 76.

Tuberculous abscess cavities injected with glycerin after evacuation of contents and cauterising with iodised phenol.—H. A. Morton-Whitby, *Brit. med. J.*, 1/1931, 206.

VARICOSE VEINS. Intravenous injections of 5 to 10 ml. of 50% glycerin and water initially, and 6 days later one or two injections of a 75% mixture. All cases successful—F. Maignon, per *Prescriber*, 1932, 34.

**WOUNDS** as arriving in Casualty Dept at a London hospital treated with a mixture of glycerin 1, liquid glucose 6 and water 3—left on 3 days, then a dry dressing with boric acid powder. Also effective in bromidrosis and in ozæna.—T H C Benians, *Brit med J*, 1/1931, 285

The addition of about 25% of glycerin to a wet dressing avoids the bleaching and maceration of the skin. The surface of the wound is kept moist, the discharge is not pent up under a scab and the wound is thus encouraged to heal from the bottom. Even when the dressing has to be applied for weeks or months the skin remains normal.—D Kyle, *Practitioner*, 11/1933, 318

### Glycerin in Labour.

**LYMPHAGOGUE ACTION** of a 10% solution of tincture of iodine in glycerin. The iodine helps to stimulate uterine contraction.—H J Phillips, *Lancet*, 11/1925, 1229, 1307, *Proc R Soc Med*, Feb, 1926, 26

In obstetrics glycerin is useful, (a) where puerperal sepsis is a possibility, and (b) mild sapræmia or definite septicæmia.—C Elliott, *Lancet*, 1/1929, 1057

**Glycerin in midwifery** advocated. It is powerfully hygroscopic, inhibits bacterial growth, particularly the cocci and coli groups, the causal organisms of puerperal sepsis, reduces œdema, and encourages healing of lacerated tissues. Soothing to hæmorrhoids. Used as routine at every confinement.—R Mackinnon, *Brit med J*, 11/1930, 980

A viscous hygroscopic fluid like glycerin, containing an antiseptic, used during labour, would diminish chance of infection from without and from the vagina. Lord Moynihan suggested acriflavine. Continuous administration of calcium salts from commencement of pregnancy to end of the puerperium advised to build up resistance—15 gr. of calcium phosphate in  $\frac{1}{2}$  oz. of water thrice daily.—J L Moir, *Brit med J*, 11/1930, 1066, 1/1931, 118

Glycerin and acriflavine (1 in 500) for torn perineum.—P G Preston, *Brit med J*, 1/1931, 294

**Glauramine** (qv) in glycerin 1 in 60 suggested in midwifery, especially when frequent examinations needed and in prolonged or difficult labour. No irritation.—F H Lacey, *Brit med J*, 1/1931, 36

**PUERPERAL SEPSIS** Glycerin irrigation (up to 200 ml. once or thrice daily into the uterine cavity or cervical canal) the most effective remedy at our disposal, but should be used at an early stage. Pyrexia as a sign for puerperal sepsis an entirely unreliable guide—it rarely develops at the outset, pulse rate of more importance. Drainage by glycerin started as soon as temperature rises to 99° or pulse rate to 90. It is not normal for a woman to suffer from after-pains for the first few days after the puerperium, and pain is invariably due to interference with free drainage. Profuse lochial discharge another indication for early treatment.—A R Hobbs, *Brit med J*, 11/1931, 746

### Enema Glycerini (B.P.C.)

**Dose.**— $\frac{1}{2}$  to 2 ounces (15 to 60 ml.). 20 to 50% v/v in water or mucilage of starch. Undiluted, 1 to 4 drachms (4 to 16 ml.)

### Glycerinum Aluminis et Acidi Tannici.

Potassium alum (free from iron), in powder, 1, glycerin 6. Heat to dissolve and add tannic acid 1. An astringent throat pigment. Diluted 1 in 20 as a vaginal injection.

### Glycerinum Boracis cum Potassii Chlorate (R.D.H.)

Potassium chlorate 20 gr., borax 10 gr., tragacanth 4 gr., glycerin 1 dr., chloroform water to 1 oz.

### Glycerinum cum Aqua Rosæ.

Glycerin 2, rose water 3. An agreeable emollient for the skin.

### Glycerin Jelly, for toilet use.

Gelatin 140 gr., rose water 6 oz., soak a few minutes and heat in a water-bath to dissolve, add, when cool but still fluid, white of egg  $\frac{1}{2}$  oz. Heat to coagulate completely, and add glycerin 6 oz., salicylic acid 12 gr. Mix well, filter through a hot-water funnel, and bottle while warm.

**Lubricant Glycerin Jelly** is somewhat softer than the latter. For toilet use and lubrication of stomach tubes.

### Glycero-alcohol. Syn PETT'S LIQUOR

**Dose.**—5 to 60 minims (0.3 to 4 ml.).

Glycerin 333, distilled water 146, alcohol 95% 580. Is used as a solvent of alkaloids and active principles. It has sp. gr. about 1.

**Suppositorium Glycerini (B.P.)** Gelatin 14, glycerin (by weight) 70, water *q s.* to 100, suitably combined. Pour into moulds of 15, 30, 60 or 120 minims or other capacities as required. Contains 70% by weight of glycerin. This basis may be used for gelatin pessaries.

**Suppositorium Glycerini Saponatum (B.P.C.)** contains 90% *w/w* of glycerin.

**Suppositoria Glycerini (U.S.P. XI)**

Dissolve 8 g of sodium stearate in 92 g of glycerin heated at 95°, add 5 g of water and pour into moulds to produce 30 suppositories.

**Vaginal Suppositories (U.S.P. XI)** are globular or oviform in shape and weigh about 5 g.

**Glycerin Tampons** consist of gauze and wool swabs soaked in medicated glycerin.

**Hollow Suppositories**, composed of oil of theobroma, may be filled with 20, 45, or 90 grains of glycerin, they are prompt in action.

**Unguentum Glycerini Compositum (St. T. H.)**

Glycerin 3 dr., strong solution of lead subacetate 20 m., wool fat 3 dr., lavender oil 1 m., yellow soft paraffin to 1 oz.

**Ethylene Glycol**, *syn* GLYCOL,  $\text{CH}_2\text{OH} \cdot \text{CH}_2\text{OH}$ , is a colourless liquid with properties intermediate between those of alcohol and glycerin. B.p. about 197°. Used as a solvent. Is non-inflammable and non-corrosive to metals. Used as an "anti-freeze" and as an ingredient in dynamite, also as a solvent for preparing flavouring essences, it is a good solvent for terpeneless oils.

As a solvent or vehicle for medicinal products it is comparatively innocuous. It is said that even 140 ml. would be needed to cause toxic symptoms in man, and the fatal dose would be more than  $\frac{1}{2}$  lb.—P. J. Hanzlik and co-workers, *J. Pharmacol.*, Apr., 1931, 406. W. F. von Ottingen and E. A. Jirouch, *ibid.*, Aug., 1931, 371, draw, however, other conclusions and say subcutaneously likely to cause irritation and large doses may cause severe gastro-enteritis.

**Ethylene glycol Monoethylether**,  $\text{C}_2\text{H}_5\text{O} \cdot \text{CH}_2\text{CH}_2\text{OH}$ , is a colourless odourless liquid with a boiling-range of 128° to 137°. Is used as a solvent.

**Diethyleneglycol Monoethylether**,  $\text{C}_2\text{H}_5\text{O} \cdot \text{CH}_2\text{CH}_2\text{O} \cdot \text{CH}_2\text{CH}_2\text{OH}$ , is a colourless hygroscopic liquid boiling at 180° to 200°. Is also used as a solvent.

**Triacetin**, *syn* GLYCERYL TRIACETATE, is a colourless liquid slightly soluble in water, b.p. about 258°. Is used as a plasticiser.

**Glycetracts.**

Glycetracts are liquid extracts prepared with a menstruum of diluted glycerin. They may be prepared by the methods given below, the strength being 1 in 1 in all cases except those which can be assayed for alkaloidal content, these are standardised to the same strengths as the corresponding alcoholic liquid extracts. For further details see W. H. Martindale, *Chem. & Drugg.*, 1/1908, 489.

1. **For drugs containing water-soluble constituents, biters, tannin principles, and some flavouring agents**—

(a) *Percolation process.* For those drugs which will percolate satisfactorily, without "blocking," this method is to be preferred. Macerate 100 of the drug in No. 20 powder in glycerin 50 and water 200 for 24 hours, then commence percolation. Reserve the first 50 of percolate and continue percolation with chloroform

water (1 in 1000) until exhausted. Evaporate the liquor to 50 and add to the reserved portion.

(b) *Maceration process.* For drugs which will not percolate satisfactorily. Macerate 100 of the crushed drug in a hot mixture of glycerin 50 and water 200 for 6 hours, press, and repeat the maceration with hot water twice. Combine the liquors and evaporate to 100.

2. **Alkaloidal Drugs.** For drugs containing alkaloids, percolate the crushed drug 100, with a mixture of glycerin 50, acetic acid 9, and water 191, and proceed otherwise as under 1 (a), making the final product 100 containing about 3% of acetic acid

### **Glyl and Syl Flavouring Agents** (*Martindale, London*).

These are solutions of essential oils in either glycerin (Glyl) or syrup (Syl) for flavouring and sweetening nauseous medicines. They are prepared with 1 of essential oil in 500 of glycerin or syrup, approximately 1 m. per oz.

Half the required amount of glycerin (slightly warmed, *e.g.*, by standing the bottle in a little hot water) or syrup is placed in a bottle capable of holding the full amount, the essential oil mixed with 3 times its volume of alcohol 90% is added in small portions, with shaking, then the remainder of the glycerin or syrup is added, with further shaking. The product is allowed to stand a short time for any excess of essential oil to rise and filtered through a pledget of moist cotton-wool. 1 to 2 dr. is usually sufficient for 1 oz. of medicine.

## **GLYCYRRHIZA**

*B.P., U.S.P. XI, P. Helv. V, P. Dan*

*Dose.*—15 to 60 grains (1 to 4 g.)

The root and subterranean stem of *G. glabra* and other species (Leguminosæ). Both the peeled and unpeeled drug is included in the *B.P.*, the latter being admitted only when expressly named, *e.g.*, for preparing the extracts. Is demulcent and expectorant

### **Elixir Glycyrrhizæ** (*U.S.P. XI*)

Fluidextract of glycyrrhiza 12 5%, in aromatic elixir.

**Liquor Pectoralis** (*P. Dan*) *Syn.* ELIXIR PECTORALE, KING OF DENMARK'S CHEST MIXTURE. *Dose.*—1 drachm. Extract of liquorice 1, fennel water 3, anisated liquid ammonia 1

*P. Svec. X* has extract of liquorice 200, fennel water 600, ammonia solution 9% 35, anise oil 2, alcohol 90% 163. [*P*1] **Liquor Pectoralis Benzolicus** (*P. Svec. X*). Tinctura Opii Benzoica 1, Liquor Pectoralis 3

### **Extractum Glycyrrhizæ** (*B.P.*).

*Dose.*—10 to 30 grains (0.6 to 2 g.).

The evaporated chloroform water percolate. Used in lozenges and pastilles.

**Extractum Glycyrrhizæ** (*U.S.P. XI*). This is the commercial extract in powder or in rolls or masses. **Extractum Glycyrrhizæ**

**Purum (U.S.P. XI)** is an aqueous extract of the rhizome and roots, of pilular consistence.

**Extractum Glycyrrhizæ Liquidum (B.P.)**

*Dose* —  $\frac{1}{2}$  to 1 drachm (2 to 4 ml.).

1 in 1, by percolation with chloroform water, evaporation, and addition of 25% of alcohol 90%. Is a useful flavouring agent, especially for ammonium chloride, alkaline iodides, cascara, magnesium sulphate, quinine sulphate, ipecacuanha and aloes, but is incompatible with acids.

**Fluidextractum Glycyrrhizæ (U.S.P. XI).**

*Average dose.*—30 minims (2 ml.) Prepared by maceration and percolation with boiling water, followed by evaporation after the addition of ammonia and then finally adding alcohol and sufficient water.

**Pulvis Glycyrrhizæ Compositus (B.P.).** *Syn* PULVIS PECTORALIS (*Kurellæ*).

*Dose* — 1 to 2 drachms (4 to 8 g) mixed with water or milk, taken early in the morning

Senna and liquorice of each 2, fennel and sublimed sulphur of each 1, sucrose 6 $\frac{1}{2}$ . Mix.

For constipation and hepatic disease, it is pleasant to take, and effectual without catharsis. *U.S.P. XI* uses oil of fennel, which makes it less granular. It is also prepared *sine Saccharo*—with half the above dose, and is more palatable.

**Poudre de Régliſſe Composée.** *Syn* PULVIS LIQUIRITIÆ COMPOSITUS (*Fr Cx*). Contains liquorice 1 $\frac{1}{2}$ , senna (washed with alcohol and powdered) 1 $\frac{1}{2}$ , fennel 1, sublimed sulphur 1, sucrose 5.

**Pulvis Sennæ Compositus (U.S.P. XI).** *Syn* PULVIS GLYCYRRHIZÆ COMPOSITUS (*U.S.P. XI*).

*Average dose* — 60 grains (4 g).

Senna 18, liquorice 23.6, washed sulphur 8, oil of fennel 0.4, sucrose 50.

**Trochisci Glycyrrhizæ (B.P.C),** *syn.* BROMPTON COUGH LOZENGES, contain 3 grains of extract of liquorice and  $\frac{1}{2}$  minim of oil of anise. These lozenges are brown in colour. Lozenges which are black usually contain charcoal.

**Pastilles de Régliſſe.**—Liquorice pastilles, much used in France.

**Glycyrrhizinum Ammoniatum.** *Dose* —  $\frac{1}{2}$  to 5 grains. Glycyrrhizin is contained in the root as the ammonium salt. Readily soluble garnet coloured shining scales. It possesses a persistent sweet taste. A grain will flavour 6 ounces of water. It may, perhaps, be considered as the ammonium salt of glycyrrhizinic acid which, according to Tschirch, has the formula  $C_{42}H_{64}O_{16}(COOH)_4$ .

In addition to the extracts, dried "liquorice juice" or "Spanish liquorice" (*Succus Liquiritiæ, P. Helv. V*) is sold, that bearing the stamp of Solazzi being most prized. Pontefract cakes of liquorice and "pipe liquorice" are useful in allaying tickling coughs.



**Abrus (B.P.C.)** *Syn* JEQUIRITY, JUMBLE BEADS, PRAYER BEADS.

The seeds of *Abrus precatorius* (Leguminosæ), a tropical climbing plant. Contains abrin, a mixture of two poisonous proteins. Infusum Abri 8% has been used, diluted, for granular eyelids.

Instillation of 5% infusion of crushed seeds for relief of pannus—Licut—Col H Kirkpatrick, *Lancet*, 1/1921, 1304

**Abri Radix, syn** INDIAN LIQUORICE, is the root of *Abrus precatorius* (Leguminosæ). It has poisonous properties and should not be used as a sweetening agent.

**Althæa (B.P.C., U.S.P. XI, P. Dan.)** *Syn* MARSHMALLOW, GUIMAUVE.

The dried peeled root of *A. officinalis* (Malvaceæ), collected from plants not less than two years old. Contains a fatty oil and 25 to 35% of mucilage. Used as a demulcent in bronchitis. The powdered root is a useful absorbent in pill-making. The leaves (*Althæa Folium P. Helv. V*) were formerly used for preparing a soothing ointment.

**Marshmallow Pastilles.** *Syn* PASTILLES DE GUIMAUVE.

Boil incised marshmallow root 100 in water 400, strain off the liquor. Evaporate to about 80 and mix with tragacanth 10 and sugar 1000, adding orange-flower water 10 or more if necessary to make a mass for cutting into pastilles weighing 20 grains (1.2 g). This basis may be medicated with throat remedies similar to those used in glyco-gelatin pastilles.

**Species Pectorales (P.G. VI)** Coarsely cut marshmallow root 8, liquorice root 3,orris root 1, tussilago farfara (coltsfoot) leaves 4, verbasum flowers 2, anise 2.

**Syrupus Althææ (B.P.C.)** *Syn* SYRUP OF MARSHMALLOW.

*Dose*— $\frac{1}{2}$  to 2 drachms (2 to 8 ml) 1 in 25.

**Cetraria (B.P.C., P. Helv. V, P. Dan.)** Iceland moss is the dried lichen, *C. islandica* (Parmeliaceæ).

Contains the carbohydrate, lichenin, and its isomeride iso-lichenin. Has demulcent properties, and is used in Northern Europe as a food.

Usually administered as *Decoctum Cetraria*, dose—1 to 4 fl ounces (30 to 120 ml.), 1 in 20; also as lozenges, the bitterness (due to cetraric acid) being removed by prolonged soaking in water.

**Marrubium (B.P.C.)** *Syn* HOREHOUND.

*Dose*— $\frac{1}{4}$  to  $\frac{1}{2}$  drachm (1 to 2 g). The dried leaves and flowering tops of *M. vulgare* (Labiata). Expectorant, laxative in large doses.

**Infusum Marrubii Concentratum (B.P.C.)** *Dose*— $\frac{1}{2}$  to 1 drachm (2 to 4 ml) 1 in 2 $\frac{1}{2}$ . This preparation diluted with 7 volumes of water may be dispensed when Infusum Marrubii is prescribed.

**Syrupus Marrubii (B.P.C.)** *Dose*— $\frac{1}{2}$  to 1 drachm (2 to 4 ml). About 1 in 2. Prepared by dissolving sucrose in an aqueous decoction of the drug.

**Symphytum (B.P.C.)** *Syn* COMFREY ROOT.

The dried rhizome and root of *Symphytum officinale* (Poraginaceæ). Contains 0.6 to 0.8% of allantoin, and has been applied to wounds and ulcers in form of a decoction (1 in 20), or as a poultice prepared from the fresh root. The liquid extract (1 in 4 by extracting the drug in coarse powder with water, and preserving with 20% of 90% alcohol) has been given internally for gastric ulcer in doses of 2 to 4 drachms.

**Allantoinum** (*B.P.C.*)  $C_4H_6O_3N_4 = 158.1$ .

*Dose* —  $\frac{1}{2}$  to 2 grains (0.03 to 0.12 g.).

A diuretic of glyoxylic acid, prepared by the oxidation of uric acid. Occurs in colourless crystals. M.p. about  $235^\circ$ .

**Soluble** 1 in 260 of water, almost insoluble in alcohol 90%.

A cell proliferant. Has been applied locally to indolent ulcers and sluggish wounds and abscesses.

**Tussilaginis Flos** (*B.P.C.*). *Syn.* COLTSFOOT FLOWER, FARFARÆ FLORES. The dried flowering shoots of *Tussilago Farfara* (*Compositæ*). Demulcent, relieves irritable cough.

**Extractum Tussilaginis Liquidum** (*B.P.C.*) *Syn.* LIQUID EXTRACT OF COLTSFOOT.

*Dose* — 10 to 30 minims (0.6 to 2 ml.) 1 in 1.

**Syrupus Tussilaginis** (*B.P.C.*) *Syn.* SYRUP OF COLTSFOOT.

Liquid extract of coltsfoot 25% v/t in syrup.

**Tussilaginis Folium** (*B.P.C.*) *Syn.* FARFARÆ FOLIA.

The dried leaves of *Tussilago Farfara*. Has been administered for its demulcent properties in the form of a decoction (1 in 20, *dose* — 2 ounces).

## GOSSYPHII CORTEX

*B.P.C.*

*Syn.* GOSSYPHII RADICIS CORTEX

The root bark of *Gossypium herbaceum* (*Malvaceæ*) and other cultivated species.

**Uses.** Preparations are given instead of ergot to check uterine hæmorrhage in all its forms. May relieve dysmenorrhœa.

**Decoctum Gossypii Corticis** (*B.P.C.*) *Dose* —  $\frac{1}{2}$  to 2 ounces (15 to 60 ml.). 1 in 5.

**Extractum Gossypii Corticis Liquidum** (*B.P.C.*)

*Dose* —  $\frac{1}{2}$  to 1 drachm (2 to 4 ml.) 1 in 1.

**Extractum Gossypii Corticis.** Semi-alcoholic.

*Dose* — 1 to 4 grains (0.06 to 0.25 g.) in pill.

**Pilula Gossypii Composita.** *Dose* — One, 3 or 4 times a day. Extract of cotton root, extract of hydrastis, ergotin, of each 1 gr.

**Tinctura Gossypii Corticis** (*B.P.C.*) 1 in 4.

*Dose* —  $\frac{1}{2}$  to 1 drachm (2 to 4 ml.)

**Lactagol** (*Lactagol, London*) is an extract of cotton seed. *Dose* — 1 teaspoonful 4 or 5 times daily given in milk.

Used to increase the flow of milk and the nitrogenous constituents of same.

**Edestine.** Stated to be the active principle, so far as galactagogue action is concerned, of cotton seed freed from fat, etc. Is also obtainable from linseed by precipitation with water from a 4% saline extractive.

Effect of edestine on mammary secretion in rats. It is a good protein sparer and improves growth, but in large proportion (e.g., 46%) the young die — *G. A. Hartwell, Lancet, 1/1922, 323.*

**Aletris** (*B.P.C.*). *Syn.* STAR GRASS, AGUE ROOT, COLIC ROOT. *Dioscorea* is also called colic root).

The dried rhizome and roots of *A. farinosa* (*Liliaceæ*). Used as so-called uterine tonic.

**Elixir Aletridis** (*B.P.C.*). *Dose.*— $\frac{1}{2}$  to 1 drachm (2 to 4 ml.).

A flavoured preparation containing 25% *v/v* of liquid extract of aletris.

**Extractum Aletridis Liquidum** (*B.P.C.*). *Dose.*—5 to 15 minims (0.3 to 0.8 ml.). 1 in 1.

**Caulophyllum** (*B.P.C.*). *Syn.* BLUE COHOSH, PAPOOSE OR SQUAW ROOT. *Dose.*—5 to 30 grains (0.6 to 2 g.).

The rhizome and roots of *C. thalictroides* (*Berberidaceæ*).

Diuretic and emmenagogue.

**Extractum Caulophylli Liquidum** (*B.P.C.*). *Dose.*—10 to 30 minims (0.6 to 2 ml.). 1 in 1.

**Liquor Caulophylli et Pulsatillæ** (*B.P.C.*). *Dose.*—1 to 2 drachms (4 to 8 ml.).

Contains 25% *v/v* of liquid extract of caulophyllum and 5% *v/v* of liquid extract of pulsatilla.

**Liquor Caulophylli et Pulsatillæ Compositus** (*B.P.C.*).

*Dose.*—1 to 2 drachms (4 to 8 ml.).

Contains liquid extracts of caulophyllum 15%, pulsatilla 5%, aletris 10%, and black haw 20% (all by volume). A sedative in dysmenorrhœa and uterine disorders.

**Caulophyllin**, *dose.*—1 to 4 grains (0.06 to 0.25 g.), is the resinoid obtained by precipitating a concentrated alcoholic tincture. Has diuretic, diaphoretic, antihelmintic, antispasmodic and emmenagogue properties.

**Helonias**. FALSE UNICORN ROOT The dried rhizome and root of *Chamaelirium luteum*. Is used in colic and in atony of the generative organs; also employed as an abortifacient.

"**Helonias Compound.**" Aloes 9 oz., helonias 14 oz., tansy 14 oz., oil of pennyroyal  $1\frac{1}{2}$  oz., oil of cassia 1 drachm, cayenne  $\frac{1}{2}$  oz., myrrh 8  $\frac{1}{2}$  oz. in 1 gallon of 17% alcohol. *Dose.*—1 drachm in a cup of hot water, sweetened, twice daily. For promoting menstruation.

A case in which a man was proved guilty of supplying a noxious drug to procure miscarriage.—*Pharm J*, 11/1924, 342.

**Placidia** (*B.P.C.*). *Syn.* JAMAICA DOGWOOD. The root bark of *P. Erythrina* (*Leguminosæ*). Useful in neuralgia, toothache, bronchitis, pertussis, insomnia, and dysmenorrhœa.

**Extractum Placidie Liquidum** (*B.P.C.*). *Dose.*— $\frac{1}{2}$  to 2 drachms (2 to 8 ml.). 1 in 1. A dry alcoholic extract, *dose.*—2 to 5 grains, is also prepared.

**Pulsatilla** (*B.P.C.*). *Syn.* PASQUE FLOWER. The dried herb, *Anemone Pulsatilla* (*Ranunculaceæ*). Contains a crystalline vesicant substance, anemone camphor. Used in dysmenorrhœa and amenorrhœa.

**Extractum Pulsatillæ Liquidum** (*B.P.C.*) *Dose.*—2 to 5 minims (0.12 to 0.3 ml.). 1 in 1.

**Tinctura Pulsatillæ** (*B.P.C.*). *Dose.*—5 to 30 minims (0.3 to 2 ml.). 1 in 10. Dysmenorrhœa relieved by pulsatilla. Not used in cases where the amount is excessive, lasting six days or more. The mixture given was Tinct. Pulsatilla 4 dr., Spt. Chlorof. 2 dr., chloroform water to 6 oz. 2 dr. to be taken as soon as menstrual (or premenstrual) pain begins and every three hours while pain continues.—*F. C. Coley, Brit. med. J.*, 1/1922, 13.

**Senecio**. RAGWORT. *Senecio Jacobæa* and *S. aureus* (*Compositæ*) are emmenagogues, and have been employed in amenorrhœa and dysmenorrhœa. Liquid Extract, 1 = 1 of herb. *Dose.*—20 to 60 minims. *Senecio cineraria* (*Cineraria maritima*) has been employed in the form of a tincture, 3 to 4 drops to an eye-bath of water, in the treatment of cataract. The fresh juice has also been used as eye-drops for the same purpose.

**Viburnum** (*B.P.C.*, *P. Helv. V*). *Syn.* BLACK HAW.

*Dose.*— $\frac{1}{4}$  to  $\frac{1}{2}$  drachm (1 to 2 g.).

The dried root bark of *V. prunifolium* (Caprifoliaceæ). Antispasmodic, diuretic and nervine sedative. Used in dysmenorrhœa and in threatened abortion for its supposed sedative effect on the uterus.

**Elixir Viburni** (*B.P.C.*). *Syn.* ELIXIR VIBURNI PRUNIFOLII

*Dose.*— $\frac{1}{2}$  to 2 drachms (2 to 8 ml). Liquid extract of black haw 1 in 8 with compound tincture of cardamom and aromatic elixir.

**Elixir Viburni et Hydrastis** (*B.P.C.*). *Syn.* ELIXIR VIBURNI COMPOSITUM

*Dose.*— $\frac{1}{2}$  to 1 drachm (2 to 4 ml).

Contains liquid extract of black haw 30 m. and extract of hydrastis about 1 gr. in 1 dr.

**Extractum Viburni** (*B.P.C.*) *Dose.*—3 to 8 grains (0.2 to 0.5 g.). A soft extract.

**Extractum Viburni Liquidum** (*B.P.C.*). *Dose.*—1 to 2 drachms (4 to 8 ml) 1 in 1.

## GOSSYPIUM

### AND OTHER ALLIED DRESSINGS.

*By rule 10 of the Poisons Rules, 1935, the provisions of the Pharmacy and Poisons Act, 1933 and of the Poisons Rules, 1935, which apply solely to substances included in the First Schedule to the Poisons Rules do not apply to surgical dressings*

**Gossypium Absorbens** (*B.P.C.*) *Syn.* ABSORBENT COTTON WOOL, GOSSYPIUM DEPURATUM (*P. Helv. V*), GOSSYPIUM PURIFICATUM (*U.S.P. XI*). The prepared epidermal trichomes of the seeds of various species of *Gossypium* (Malvaceæ). The filaments each consist of a single cell 2 to 4 cm. long forming a flattened tubular band. It is required to be not more neppy than a standard sample, and to comply with a test for absorbency. Cotton wool is soluble in an ammoniacal solution of copper oxide.

**Bandages** are made termed black cloth, buttercloth, calico, "cataract" (of special form for bandaging after the operation), crêpe, crêpe (Velpéau), crinoline (for silicating and plaster of Paris), domette, elastic circular stocking (stockinette), elastic (india-rubber webbing), flannel, gauze, muslin (for plaster of Paris), open weave (absorbent), plaster of Paris, selvedge (white and grey) and triangular splint.

**Ligamentum Crispi** (*B.P.C.*). *Syn.* CRÊPE BANDAGE. A characteristic fabric of plain weave in which the warp threads are of cotton and wool, and the weft threads are entirely of cotton. When fully extended the length is not less than twice the unstretched length, and after being stretched for 1 minute it returns to not more than two-thirds the fully-extended length.

**Ligamentum Domettæ** (*B.P.C.*). DOMETTE BANDAGE. A union fabric of plain weave in which the warp yarns are of cotton and the weft yarns of wool.

**Ligamentum Lanulæ (B P C.)** FLANNEL BANDAGE A raised fabric of plain weave made entirely of wool

**Ligamentum Linæ (B.P.C.).** BLEACHED CALICO BANDAGE. A bleached cotton cloth of plain weave

**Ligamentum Linæ Crudum (B P C)** UNBLEACHED CALICO BANDAGE An unbleached cotton cloth of plain weave

**Ligamentum Sindonis (B P C)** MUSLIN BANDAGE A cotton cloth of plain weave known as butter cloth material.

**Ligamentum Textum Apertum (B P C.)** OPEN-WOVE BANDAGE. *Syn* WHITE OPEN-WOVE BANDAGE Cotton cloth of plain weave

**Battista (B P C)** BATTISTE A bleached cotton fabric proofed on both surfaces with a rubber solution rendering it impervious to water and forming a non-adhesive surface It is heat vulcanised and not cold cured

**Billroth's Cambric.** Cotton fabric treated by a special process It takes the place of gutta-percha tissue and oiled silk, being sterilisable

**Carbasus Absorbens (B.P C)** ABSORBENT GAUZE *Syn* UN-MEDICATED GAUZE Cotton cloth of plain weave containing per inch not less than 19 threads in the warp and not less than 15 in the weft It complies with a test for absorbency

**Carbasus Absorbens in Tænia (B P C)** ABSORBENT RIBBON GAUZE. A material similar to the preceding but containing per inch not less than 30 threads in the warp and not less than 35 in the weft

The following medicated ribbon gauzes are made in  $\frac{1}{4}$ ,  $\frac{1}{2}$ , 1 and 2-inch widths, in 12 yard lengths.—Alembroth, aluminium acetate, boric acid, iodoform, [P1] mercury and zinc cyanide, [P2] mercuric chloride, [P2] phenol

**Tulle Gras (Lumière, Paris, Anglo-French Drug Co, London)** Surgical dressing consisting of wide-mesh gauze impregnated with soft paraffin and 1% balsam of peru, and sterilised

**Cellulosum Ligni (B P C.).** CELLULOSE WADDING *Syn*. TILLMAN'S DRESSING Is prepared from high-grade bleached sulphite pulp and complies with a test for absorbency

**Charta Oleata (B P.C).** OILED PAPER.

White paper rendered waterproof by treatment with a drying oil

**Jaconettum (B P C)** JACONEI. A bleached cotton fabric, proofed on one side with a rubber solution rendering it impervious to water and forming a non-adhesive surface. It is heat vulcanised and not cold cured Pink jaconet, coloured with a suitable dye, is also available

**Lana (B P C.)** *Syn* ANIMAL WOOL, LAMB'S WOOL Wool is the fleece of the sheep prepared by cleansing to remove grease and

other foreign substances. It consists of solid cylindrical hairs soluble in 4.5% aqueous sodium hydroxide, insoluble in ammoniacal copper oxide solution which stains it blue.

**Linteum Absorbens (B.P.C.).** ABSORBENT LINT *Syn.* LINT, COTTON LINT, UNMEDICATED LINT, LINTEUM CAPTUM. A cotton cloth of plain weave from the warp yarns of which a nap has been raised. It complies with a test for absorbency.

Lint is also obtainable medicated with iodoform 10%, and with ferric chloride 10% (styptic lint).

**Sponges, Carbolised,** have fallen into disuse but some surgeons still prefer them to cotton swabs. They are available thin and flat and can be kept in 1 in 20 phenol solution.

Sponge is the cleaned skeleton of a marine animal, *Spongia officinalis*.

**Spongio-Piline.** Thick felt with waterproof india-rubber backing for applying warm moist dressings.

**Impermeable Piline.** One-third the thickness of spongio-piline of felt, and instead of the waterproof india-rubber backing of the former, there is an antiseptic material, not affected by heat or strong spirit. For applying liniments in rheumatism, and where warmth is desired simultaneously.

**Stupa (B.P.C.) Tow** *Syn.* UNMEDICATED TOW

Jute fibre of good average quality in cheese rolls.

**Tela Carbasi et Gossypii (B.P.C.)** GAUZE AND COTTON TISSUE *Syn.* ABSORBENT GAUZE TISSUE

Consists of a thick layer of absorbent cotton wool enclosed in tubular absorbent gauze. It is also prepared medicated with boric acid, trinitrophenol, iodoform, (P2) mercuric iodide, (P1, mercury and zinc cyanide, (P2) phenol or thymol.

**Eye Pads** are ready cut, round or oval, consisting of a layer of wool between two sheets of gauze.

**Tela Carbasi et Ligni (B.P.C.)** CELLULOSE TISSUE *Syn.* GAUZE AND CELLULOSE WADDING TISSUE

Consists of a thick layer of cellulose wadding enclosed in tubular absorbent gauze.

**Dental Dressings.**

For dental use are prepared --

**Aseptic Dental Napkins.**

**Absorbent Dental Rolls.** As a substitute for the napkin or rubber dam. For covering the mouths of the salivary ducts, a section may be placed on either side of a tooth, or the entire roll may be bent round the outside of the arch or under the tongue. No. 1, diameter  $\frac{5}{8}$  inch, No. 2,  $\frac{7}{8}$  inch, No. 3,  $\frac{1}{2}$  inch, No. 4,  $\frac{1}{4}$  inch, in  $1\frac{1}{2}$  or 6 inch lengths.

**Non-absorbent Dental Rolls.** To replace the rubber dam. In crown and bridge work. May be used in connection with the saliva ejector.

**Sterilised Absorbent Pledgets** for wiping out cavities.

**Aseptic Absorbent Points** are prepared for drying pulp canals.

**Sterilised Bibulous Paper**, in sheets, 3 inches by 10 inches.

**Carbolised Cotton** for filling pulp canals, and for treatment of exposed pulps.

*For descriptions of medicated surgical dressings, see under individual medicaments (also Index).*

**Sphagnum.** *Syn* TURF MOSS, BOG MOSS. The dried moss, numerous varieties of which are indigenous to Gt. Britain. Is used as an absorbent dressing and for other purposes where absorbency is required. It has the advantage that the absorbed liquid does not merely wet the surface but is absorbed into the cells of the moss which therefore does not feel wet. The plant in its dry condition will absorb upwards of 20 times its weight of water or discharge. For taking up urinary discharge in bladder, kidney and dropsical affections the material is pre-eminently suitable. The dressing is also useful as a bedding for insane persons.

**Cavendish Moss Sheets** (*Martindale, London*) are sheets of compressed sphagnum, 24 by 15 inches by  $\frac{1}{8}$  inch approximately in thickness. Gauze-covered moss, loose moss dressings, moss pillows and [P2] sublimated moss (0.25% of mercuric chloride) are also available.

**Sanodora Moss Sheets** (*Martindale, London*) are impregnated with various essential oils: bergamot, birch tar, camphor, clove, citronella, eucalyptus, citriodora, lemongrass, sassafras and wintergreen. They are used for absorbing objectionable odours and perfuming the atmosphere in closets, cloak-rooms, kitchens, factories, warehouses, etc.

**Laminaria Digitata** *Syn* SEA TANGLE. From this seaweed "laminaria tents" are made for gynecological and surgical use. Placed in contact with moisture they swell to three times their original size in dry state. The laminaria is sterilised by drying after immersion in acetone, chloroform or alcohol 90% under pressure at 133°, or by placing in saturated solution of iodoform in ether or in sublimate solution.

**Stipes Laminariæ** (*P. Helv. V*) is from *L. hyperborea* and consists of the pseudo petiole. *P. Dan* admits both *L. digitata* and *L. hyperborea*.

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## GUAIAACUM

**Guaiaci Lignum** (*B.P.C.*). *Syn.* LIGNUM VITÆ

The heartwood of *Guaiacum officinale* and of *G. sanctum* (Zygophyllaceæ). Contains 18 to 25% of resin.

**Guaiaci Resina** (*B.P.C., P. Helv. V*).

*Dose.*—5 to 15 grains (0.3 to 1 g.).

The resin obtained from guaiacum wood, in rounded tears often covered with a green powder.

**Soluble** almost completely in ether, chloroform, dehydrated alcohol, and in sal volatile and alkalis.

**Uses.** In chronic rheumatism and lumbago, and for chronic sore throats; added to purgatives is useful in gout and for sluggish liver. It is a laxative in itself.

For dysmenorrhœa, 10 gr. of the resin 3 times a day. If this causes flatulence or colic add to each dose 1 gr. of Dover's powder. The patient should begin taking it a week before the period.

It is also given to relieve amenorrhœa

**Confectio Guaiaci Composita** (*B.P.C.*) *Syn.* CHelsea PEnSIONER. *Dose.*—1 to 2 drachms (4 to 8 g.)

Guaiacum resin 1%, rhubarb 2%, sulphur 14.5%, with potassium acid tartrate, nutmeg and honey

**Jephson's Powder.** Precipitated sulphur 2, guaiacum resin 1. For tonsillitis, acne and constipation

**Mistura Guaiaci** (*B.P.C.*) *Dose* — $\frac{1}{2}$  to 1 ounce (15 to 30 ml.). Contains about 11 gr. of guaiacum resin per oz.

**Tabellæ Guaiaci et Sulphuris** (*B.P.C.*) contain 3 gr. each of sulphur and guaiacum resin

**Tinctura Guaiaci** (*B.P.C.*) *Dose* — $\frac{1}{2}$  to 1 drachm (2 to 4 ml.) 1 in 5

**Tinctura Guaiaci Ammoniata** (*B.P.C.*)

*Dose* — $\frac{1}{2}$  to 1 drachm (2 to 4 ml.).

1 in 5, in an ammonia-alcohol solvent with oils of lemon and nutmeg

This is very useful where the uvula and fauces are enlarged. When dispensed in mixtures the resin must be suspended with 1 in 8 of mucilage of tragacanth

**Trochisci Guaiaci Resinæ** (*B.P.C.*) Contain 3 grains of guaiacum resin with fruit basis

## HAMAMELIS

**Hamamelidis Cortex** (*B.P.C.*), *syn* WITCH HAZEL BARK, is the bark of *Hamamelis virginiana* (Hamamelidaceæ), and contains about 6% of tannin. It is imported from the United States

**Uses.** To check hæmorrhages and excessive mucous discharges, and for piles

**Tinctura Hamamelidis** (*B.P.C.*)

*Dose* — $\frac{1}{2}$  to 1 drachm (2 to 4 ml.) 1 in 10 of alcohol 45%.

Was formerly given to check bleeding from the lungs or other organs but the tannin is converted into sodium gallate on reaching the blood—this substance has no remote astringent action. Large doses, *e.g.*, 1 drachm every 2 hours up to 4 oz. during the period, are, however, stated to be effectual in menorrhagia

$\frac{1}{2}$  drachm of the tincture in 1 ounce of cold water may be given as a retention enema for bleeding piles every day.

A lotion of 1 or 2 dr. with water to 1 oz. is a useful application to bruises and small wounds.

**Hamamelis** (*B.P.*, *P. Helv.* V) *Syn.* HAMAMELIDIS FOLIA, WITCH HAZEL LEAVES.

Consists of the dried leaves of *Hamamelis virginiana*.



**Extractum Hamamelidis (B.P.C.).** *Syn* HAMAMELIN, HAMAMELIDIN. *Dose*.—1 to 5 grains (0.06 to 0.3 g.) in pill.

A dry alcoholic extract from the leaf. It may be brown or green in colour according to the leaf from which it is prepared and the temperature of evaporation.

A suppository of 1 to 3 grains with cacao butter is useful for piles

**Extractum Hamamelidis Liquidum (B.P.)**

*Dose* —  $\frac{1}{2}$  to 1 drachm (2 to 4 ml.).

A 1 in 1 preparation of the dried leaves made with 45% alcohol.

HÆMORRHOIDS well treated by interstitial injection of 2 to 5 minims of a 10% solution of phenol in liquid extract of hamamelis. A patient who had suffered for a year required 7 injections—another case of 15 years' duration needed only 5. The greater the number of piles, the greater the number of treatments required. Patients stated that their rectal and general condition was greatly improved after the first injection.—J. Dunbar, *Brit. med. J.*, 11/1923, 808.

[P2] **Sterules of Hamamelis and Phenol** (*Martindale, London*) contain 0.5 ml. of liquid extract of hamamelis containing 10% of phenol

**Liquor Hamamelidis (B.P.C.).** *Syn* DISTILLED WITCH HAZEL. *Dose* —  $\frac{1}{2}$  to 3 drachms (2 to 12 ml.) 1 in 1, prepared by distillation from the fresh leaves. Used externally for piles, and by rectal injection for internal piles, to check epistaxis and bleeding from tooth sockets, also for application to bruises.

For piles, 5 minims of a mixture of equal parts of the liquor and glycerin containing 10% of phenol, have been injected into the piles hypodermically.

**Pasta Hamamelidis (B.P.C.)** *Syn* WITCH HAZEL CREAM

A non-greasy stearate cream containing about 50% *w/w* of solution of hamamelis

**Cremer Hamamelidis (L.H.)** Solution of hamamelis 60 m, yellow soft paraffin 120 gr., wool fat to 1 oz.

**Hazel Foam** (*Martindale, London*) A soothing, non-greasy ointment basis. May be medicated with all forms of antiseptics and skin applications, e.g., ichthammol 3%; ichthammol 3 to 10% with resorcin 5%, salicylic acid 1%, cade oil 5%, phenol 1 to 2½%, solution of coal tar 10%.

**Suppositorium Hamamelini et Zinci Oxidi (B.P.C.)** contains 3 gr. of extract of hamamelis and 10 gr. of zinc oxide with oil of theobroma to 30 gr.

[D P1 81] **Compound Hamamelis Suppository.** Hamamelin 1 gr., orthocaine 5 gr., cocaine hydrochloride  $\frac{1}{2}$  gr., extract of opium  $\frac{1}{2}$  gr., extract of belladonna  $\frac{1}{2}$  gr., oil of theobroma to 60 gr. For internal hæmorrhoids.

[P1 81] **Suppositorium Hamamelini, Conii et Eucalinæ.**

Hamamelin 5 gr., extract of conium 4 gr., benzamine  $\frac{1}{2}$  gr. in glycerin suppository mass to 30 gr. Rub down the drugs first with a very little warm water. In painful hæmorrhoids.

[D P1 81] **Suppositorium Hamamelini et Hydrargyri Compositum.**

Mercurial ointment 1 gr., hamamelin 2 gr., extract of ergot 1 gr., extract of belladonna  $\frac{1}{2}$  gr., morphine sulphate  $\frac{1}{2}$  gr., tragacanth q.s., oil of theobroma to 15 gr.

The ingredients were prescribed by the late Campbell Williams with following intent:—The mercury to act on prostatic hyperæmia often present with piles, hamamelin on the mucous membrane, ergot on the muscular walls of blood vessels, belladonna the same and sedative, morphine analgesic and vasoconstrictor. The theobroma oil as local mechanical lubricant and the tragacanth for consistency.

**Unguentum Hamamelidis (B.P.C.).** Contains 10% of the liquid extract. It is largely employed for piles. It may be filled into hollow suppositories. A combination [D-P1-81] with cocaine 2% is useful.

[P1] **Hæmorrhaline (Hewlett, London)** An ointment for hæmorrhoids containing lead acetate, witch hazel, morphine and lanolin.

**Ficaria (B.P.C.).** *Syn* PILEWORT, LESSER CELANDINE The fresh herb *Ranunculus Ficaria* (Ranunculaceæ) An old remedy for hæmorrhoids.

**Unguentum Ficarise (B.P.C.)** is prepared by digesting the herb in benzoated lard. Suppositories are also prepared from a mass made by melting together 4 parts of ointment and 1 part of spermaceti

**Lawsonia (B.P.C.)** *Syn* HENNA The powdered leaf of *L. alba* (Lythraceæ) It is employed as a hair dye. In some cases cupric chloride and pyrogallol are used in conjunction with henna, and again borax is occasionally used as an adjuvant, the idea being no doubt that the pyrogallol oxidises more readily in alkaline solution. The quantities relative to the henna in such cases are exceedingly small.

**Sambucus (B.P.C., P. Helv V, P Dan.)** *Syn* ELDER FLOWERS. The fresh or dried corollas and stamens of *S. nigra* (Caprifoliaceæ). An infusion is a domestic remedy for bruises, etc., also a pomade prepared by digesting the flowers in melted lard.

**Sambuci Follum** were formerly used for the preparation of **Unguentum Sambuci Viride** by digestion in lard and also of **Oleum Sambuci Viride** by digesting 1 of bruised fresh leaves in 3 of linseed oil

**Aqua Sambuci (B.P.C.)** Triple elder-flower water diluted, immediately before use, with twice its volume of distilled water

**Aqua Sambuci Triplex (B.P.C.)** The undiluted elder-flower water of commerce consisting of a saturated solution of the oil

**Unguentum Sambuci (B.P.C.)** Triple elder-flower water 20% in simple ointment, coloured with chlorophyll

## HEPAS

### (LIVER EXTRACTS, AND STOMACH PRODUCTS)

The use of liver in the treatment of pernicious anæmia was founded on the observation (Whipple and co-workers, *Amer. J. Physiol.*, 1920, 53, 36) that the administration of liver to dogs which had been subjected to a hæmorrhage markedly accelerated the regeneration of blood. Successful experiments on human subjects with pernicious anæmia were described first by Minot and Murphy (*J. Amer. med. Ass.*, 11/1926, 470). The diet advocated included about  $\frac{1}{2}$  lb. of cooked liver daily and was rich in proteins, iron, vegetables and fruit, and poor in fat. These results were confirmed and extended by Minot and Murphy (*Brit. med. J.*, 11/1927, 674), and others. The liver may be given either cooked or raw. In the former case it may be cooked by any convenient method, but must not be subjected to prolonged boiling. Raw liver may be cut up into pieces and taken in cachets.

Following confirmation of the value of liver in the treatment of pernicious anæmia attempts were made to produce active extracts so as to avoid the difficulty of taking the large quantity necessary

and also the tendency to produce nausea. Beginning with the work of Cohn (*J Biol Chem.*, 1927, 74, 69), who prepared an active extract known as "Fraction G," successive investigations have resulted in the production of extracts of increasing potencies.

For further details of early work on liver treatment see G R Minot's Nobel Lecture, "The Development of Liver Therapy in Pernicious Anæmia," *Lancet*, 1/1935, 361.

### **Extractum Hepatis Siccum (B P.)**

**Dose.**—The quantity equivalent to about  $\frac{1}{2}$  lb. (225 g) of fresh liver.

It is difficult, if not criminal, to lay down any hard-and-fast rules concerning dosage. Response in different people is extremely variable. Orally, some patients require extract made from 3 lbs. of liver a day while others respond satisfactorily to a similar extract from  $\frac{1}{2}$  lb. of liver and there is the same variability in response to parenteral administration. Moreover, extracts vary enormously in potency—even with two batches of extract prepared by the same process one may be active and the other not, and an extract made from 6 g of liver may be more potent than one made from 100 g —Janet Vaughan, *Lancet*, 11/1933, 64.

A selected fraction of an alcoholic extract of ox or sheep liver containing the specific principle active in pernicious anæmia. It contains not less than one-eleventh its weight of sodium chloride and occurs as a light brown hygroscopic powder with a meat-like odour and taste. A method of preparation, originally published by the Medical Research Council, is described in the *B P.* See also J. B. Collip, *Canad. med. Ass. J.*, 1/1928, 392.

**Home-made Liver Extract.** Extract 10 oz of minced beef liver with cold water. Precipitate inert proteins by boiling and strain off. The clear yellow liquid obtained equals in activity the original amount of liver when ingested. Volume of liquid should be about 18 oz —*Pharm J.*, 11/1931, 50.

**Uses.** The administration of liver or of liver extract to pernicious anæmia patients produces a rise in the red blood cell count and a slower improvement in spinal cord symptoms. The furred tongue and diarrhœa disappear, but gastric acidity does not return and the administration of hydrochloric acid should be continued. The general health and strength of the patient return to normal except for severe cord symptoms. The reticulocytes, which are usually less than 2% before treatment, show an increase by the fourth day after commencing liver therapy and reach a peak between the seventh and tenth days; the height of the peak is inversely proportional to the initial red cell count. From an initial red cell count of 1 million a reticulocyte peak of 40% may follow; from 2 million red cells the peak may be 20%, but initial red cell counts of over  $3\frac{1}{2}$  million do not show any rise in reticulocytes. Within 3 weeks after the commencement of the treatment the reticulocyte count falls to normal level. A rise in hæmoglobin and red blood cell count usually occurs shortly after the reticulocyte peak and approximately normal values are obtained in 1 to 2 months.

**Extractum Hepatis (U.S.P. XI)** The dried soluble fraction of mammalian livers. It must be approved by the U.S.P. Anti-anæmia Preparations Advisory Board; clinical data must be supplied of cases of treatment of Addisonian pernicious anæmia and

this data must show satisfactory results when the preparation was given in the dose stated on the label.

### **Extractum Hepatis Liquidum (B.P.).**

*Dose* —1 oz. (30 ml.), equivalent to about  $\frac{1}{4}$  lb. (240 g.) of fresh liver.

The extract obtained as described for Ext. Hepatis Siccum in the B.P. is dissolved in a menstruum such that the product contains per litre the equivalent of 8000 g. of the original liver, not less than 10% v/v of alcohol 95% and not less than 20% v/v of glycerin.

### **Liquor Hepatis (U.S.P. XI)**

Like the dry extract, it must be approved by the U.S.P. Anti-anæmia Preparations Advisory Board.

**Belladonna poisoning** following the ingestion of liquid extract of liver. In a quantitative examination, 5 mg. of alkaloid was obtained from 2 oz. of extract. The possibility of contamination was strongly denied by the manufacturers and the suggestion was made that belladonna leaves and fruit had been eaten by the animals from whose livers the extract was manufactured, probably shortly before being slaughtered. The desirability of submitting each batch of liver extract to a test for alkaloids before placing on the market seems deserving of consideration —N. F. Winder and C. H. Manley, *Brit. med. J.*, 1/1936, 413.

**Fish Liver Extract.**—An extract made from whiting, haddock and cod livers has been shown to be of remarkable potency in the treatment of pernicious anæmia, the red cell count and hæmoglobin percentage being doubled or trebled within a few days. Whiting-liver extract is more pleasant to take than that from haddock or cod, and is similar to but nicer than mammalian liver extract. The daily dose during the acute stage is the extract of 1000 g. of raw fish liver (= 500 g. of liver tissue) —L. S. P. Davidson, *Brit. med. J.*, 11/1932, 347.

**Assay.** At present the only available method for the assay of liver extracts is a clinical test involving the determination of the reticulocyte response in untreated cases of pernicious anæmia. The statement that a given quantity of liver extract is derived from a stated amount of fresh liver may be misleading since loss of potency may occur in the process of manufacture.

**Standardisation of Liver and Stomach Preparations for use in the Treatment of Pernicious Anæmia.**—A STATEMENT BY THE COUNCIL ON PHARMACY AND CHEMISTRY OF THE A.M.A.—Standardisation of preparations depends on the reticulocyte response following the uniform daily administration of the product to a patient with pernicious anæmia. The test patient should preferably have no complicating infection, diarrhœa, marked arteriosclerosis or extensive neurologic changes. The red blood cell count should be between 1,000,000 and 3,000,000 per cubic millimetre and the patient should not be in a spontaneous or induced remission, nor should transfusion have been performed recently. The patient should not have received potent antianæmic material or arsenic within a month. Daily reticulocyte counts for one day before and ten days after the test has been started should be made. During days of marked rise of reticulocytes, two counts a day may be necessary to determine the maximal value. The acceptable standard response is set forth in the accompanying table.

<i>Initial Red Blood Cell Count, Million per Cu. Mm.</i>	<i>Minimum Reticulocyte Response, Per Cent</i>
1.0	30
1.5	18
2.0	12
2.5	7
3.0	4

The figures given have been obtained by the daily oral administration of material derived from 300 to 400 g. of liver, or 30 to 40 g. of desiccated stomach,

or by the daily parenteral injection of material derived from 10 to 15 g. of liver.

The test should be conducted by uniform daily administration for ten days of the least amount of material expected to yield the standard reticulocyte response. Should there be no reticulocyte response or a lesser response than the required minimum, within the ten-day period, that amount of a preparation of established potency known to correspond to the foregoing standards should be administered in uniform dosage for ten days. The purpose of this control is to establish the reactivity of the patient to known amounts of active principle. In assaying an orally administered product an orally administered standard should be used, and with a product for parenteral use a parenterally administered standard should be employed. The principles underlying the determination of potency of autolysed liver preparations, stomach tissue extracts or combinations of liver and stomach tissue or extracts are the same. In each case the least daily amount of the preparation administered that is necessary to produce the reticulocyte response within the ten-day period should be determined. Satisfactory responses to similar tests should be obtained in at least three patients.—*J. Amer. med. Ass.*, ii/1935, 319. See also G. R. Minot and W. B. Castle, *Lancet*, ii/1935, 319.

**Liver Extracts for Parenteral Administration.** In a small percentage of cases oral administration of liver or of extracts of liver fails to produce a reticulocyte response, possibly due to the wall of the intestine being abnormally impermeable to the active principle. Attempts were therefore made to administer liver extracts by injection. The early extracts were unsuitable for administration in this way owing to the presence of too much protein and of a principle which caused a fall in blood-pressure and which it was not found possible to remove to a sufficient extent. In 1931, W. B. Castle and F. H. L. Taylor (*J. Amer. med. Ass.*, i/1931, 1198; *Lancet*, i/1931, 857) further purified Cohn's Fraction G (p. 518), obtaining a preparation active when given intravenously. To avoid the objections to intravenous administration, a further preparation was obtained (M. B. Strauss, F. H. L. Taylor and W. B. Castle, *J. Amer. med. Ass.*, ii/1931, 313) of which 2 ml., equivalent to 10 g. of liver, was given daily by intramuscular injection. In general, extracts for parenteral administration are prepared from an aqueous extract of fresh minced liver by precipitation of proteins and other extraneous matter by means of heat and fractional precipitation with alcohol. Finally the active fraction is precipitated by alcohol 95% and may be dissolved in water and the solution sterilised, an antiseptic being usually added.

**Liquor Hepatis Purificatus (U.S.P. XI)** is the liquid extract or solution prepared for injection; it must be sterile and may contain not more than 0.5% of cresol or phenol.

There is no doubt at all that for the treatment of pernicious anaemia the use of fresh liver or oral liver extracts does not give as good results as stomach preparations or parenteral liver extracts. Extracts for intravenous injection should only be used which have been guaranteed by the manufacturers to have been clinically tested and found active in the treatment of pernicious anaemia. Price is no criterion and fortunately most of the cheapest preparations are more active than many of the most expensive ones.—J. F. Wilkinson, *Practitioner*, ii/1933, 412.

It is possible to state without hesitation that intramuscular treatment (as opposed to oral treatment) given at intervals of 2 or 3 weeks, is the cheapest and best method for maintaining a normal blood level in pernicious anaemia.—S. Davidson, *Med. Annu.*, 1935, 19.

Comparison of liver extracts for parenteral use. Some showed loss of 50% of potency as a result of refining in manufacture. Manufacturers should indicate the dose necessary to produce maximum reticulocyte response.—Dameshek and Castle, *J. Amer. med. Ass.*, ii/1934, 802.

The dosage of injectable liver extracts should be thought of in terms of raw liver orally. The injectable preparation is 20 to 40 times more effective than the oral, hence 1 ml. of extract derived from 5 g. of raw liver actually represents 100 to 200 g. of raw liver. It is a safer plan to use a ratio of 20 in calculating the dosage.—E. A. Sharp, *J trop. Med. (Hyg)*, 1936, 53 and 65

## REFERENCES TO THERAPEUTIC USES OF LIVER EXTRACTS, ORAL AND PARENTERAL

For earlier references to treatment of pernicious anæmia with liver see 20th Edn., pp 951 and 952. For a summary of recent work see Prescriber, 1936, 49.

For differential diagnosis the following classification is sufficient (1) pernicious anæmia, (2) idiopathic hypochromic anæmia, (3) other deficiency anæmias, (4) hæmolytic anæmias; (5) secondary anæmias, due to malignant disease, infections or hæmorrhage, (6) aplastic anæmia, (7) splenic anæmia—J C Matthews, *Brit. med J*, ii/1935, 943

Classification and differential diagnosis of the anæmias—R L Haden *J Amer. med Ass*, i/1935, 706

AGRANULOCYTIC ANGINA Treatment by liver extract orally and parenterally, remissions occurred in five cases—Foran-Sheaff and Trimmer, *J Amer med Ass*, i/1933, 1917.

DIABETES Liver was regarded as unsuited for diabetics because of its glycogen content, it is now known to contain a blood-sugar reducing substance when taken by mouth, non-toxic and with effect similar to insulin 180 g. of raw liver may have an effect on blood sugar of diabetics equal to that from 10 to 15 units of insulin—H Blotner and W P Murphy, *J Amer med Ass*, i/1929, 1336 The preparation made on the lines indicated by Blotner and Murphy had no effect on diabetes—R D Lawrence, *Lancet*, ii/1930, 1179

DISSEMINATED SCLEROSIS treated by liver, lightly cooked,  $\frac{1}{2}$  lb daily, with remarkable results Method evolved in the hope that the nervous system might benefit, on the lines of pernicious anæmia—A Goodall and J K Slater, *Brit med J*, i/1931, 789

HÆMOPHILIA Value of liver treatment demonstrated by Pickering—*Brit med J*, i/1931, 33

SECONDARY ANÆMIA In pernicious anæmia it is an established treatment In some cases of secondary anæmia the therapy is effective in producing reticulocyte response and raising blood count Best results after hæmorrhage Give iron simultaneously, e g, Pil Ferri, 5 gr, three times a day—S C Dyke, *Lancet*, i/1929, 1192, 1206 Liver of little value—*Lancet*, ii/1930, 704

A combination of liver extract by intramuscular injection and Ferri et Annon Cit by mouth gave best results, the average daily gain in hæmoglobin being 153 mg.—W. P. Murphy, *Arch Intern. Med*, 1933, ii, 656

SMALL POX A series of 28 cases of smallpox is reported as having been treated by liver extract injections, the first of 5 ml as soon as possible, followed by two or three similar daily injections and later by 2 ml injections until eight or ten have been given. It is claimed that the duration of disease is shortened, the eruption is aborted, subsequent scarring avoided, and systematic disturbances minimised—V G Nair, *J Indian med. Ass*, 1935, 488

SPRUE Intravenous injection of liver extract in doses equivalent to 50 g of liver daily effective in the treatment of sprue.—Rhoads and Miller, *J Amer med Ass*, ii/1934, 387.

In London, at least 90% of patients with tropical sprue get completely well on combined liver extract *per os*,  $1\frac{1}{2}$  lbs (700 g) daily, and graded high protein, low fat, and low carbohydrate diet, in the ratio 1.0 to 0.3 to 1.3, respectively commencing with 500 calories and working up to 3000—N. Hamilton Fairley, *Proc Mayo Clin*, 1936, 190.

SUBACUTE COMBINED DEGENERATION. Complete arrest of the neural lesions occurred in 26 patients with advanced subacute combined degeneration of the spinal cord treated with liver extract by intramuscular injection for a period of thirty-four months (average). By appropriate treatment with parenteral liver extract the spinal cord lesions can be prevented from developing or, if present, may be completely cured.—M. B. Strauss and associates, *J. Amer. med. Ass.*, i/1935, 1587.

The most important point in treating patients with spinal cord involvement is the maintenance of the blood at or above normal level, for even with the red blood counts as high as 4 millions the development of cord lesions has been observed, while with red cells at 5 millions or higher this has not taken place—B. M. Fried, *J. Amer. med. Ass.*, 1/1929, 1260.

The point of view which has been advanced that while nerve lesions may improve, spinal cord lesions do not, is hardly in keeping with the disappearance of the Babinski reflex and ataxia. The rate of improvement in spinal cord symptoms is inversely proportional to their duration, the outlook for complete recovery being much brighter if symptoms have been present only for a few months; but even those of years' duration may show improvement with prolonged intensive treatment—R. West, *J. Amer. med. Ass.*, 11/1935, 432.

THROMBOPENIC PURPURA of moderately severe grade with oozing from gums and ecchymoses rapidly yielded to liver treatment—F. H. Jacob, *Brit. med. J.*, 1/1931, 33.

### PROPRIETARY LIVER PREPARATIONS

**Campolon** (Bayer Products, London) Liver extract for intramuscular injection 2 ml = 500 g. of liver *per os*

**Erythgen Liver Extract** (Carrick, Newark, N. J., Brooks & Warburton, London). Dose—1 to 4 drachms thrice daily Capsules, 1 to 4 thrice daily

**Exhepa** (Bencard, London) Brand of dried liver extract

**Feramin** (Duncan, Flockhart, Edinburgh) Each oz. contains the active anti-anæmic principles of 4 oz. of fresh liver, with vitamin B, and iron and ammonium citrate. Dose—In secondary anæmia, 2 tablespoonfuls twice daily, as a general tonic, 2 teaspoonfuls twice daily.

**Ferronovin** (Promonta, Hamburg, Pharmaceutical Products, London) Preparation containing liver extract, vitamin D, iron oxide, copper glycerophosphate, and soluble calcium salts, in powder or pastilles. Dose—1 to 2 teaspoonfuls of powder or 2 to 3 pastilles thrice daily

**Filivex** (Glaxo Laboratories, London) Liquid extract of fish livers. Each fluid ounce is therapeutically equivalent to the extract from 4 ounces of fresh mammalian liver. Dose.—A usual daily maintenance dose is 2 ounces.

**Hepamult** (Norgine, Prague, Napp, London) Standardised liver extract in palatable granular form (10 g = 8 oz. of fresh liver). Dose—10 to 20 g. daily.

**Ferro-Hepamult** is Hepamult with 1.7 g. of iron in 10 g.

**Heparmone** (Lilly, London) A sterile refined solution prepared from liver for the treatment of eclampsia. Dose—10 ml. or more intramuscularly (or intravenously in emergency)

**Hepastab** (Boots, Nottingham) Liver extract for intramuscular injection. Dose—4 ml. daily for 3 days, then 2 ml. daily for the next 3 or 4 days, maintenance dose, 2 ml. at intervals of 2 to 6 weeks.

**Hepatex** (Evans, Sons, Lescher & Webb, Liverpool) A liquid extract. Dose—1 dr. = 2 oz. fresh liver. **Hepatex P.A.F.** A purified and potent extract (5 ml = 100 g. of fresh liver) given intravenously and intramuscularly. Practically free from protein and does not affect blood pressure. Dose—5 ml. undiluted injected in 2 to 2½ minutes, either per week or per day, according to severity of case. **Neo-Hepatex** is a potent extract for intramuscular injection. Dose—In mild cases, 1 to 2 ml. on each of 3 successive days, then 2 ml. at 7 to 10 day intervals, in severe cases, 4 ml.

**Hepatopson** (Promonta, Hamburg, Pharmaceutical Products, London) Liver extract preparations. **Hepatopson Liquidum**, 100 ml. = 1000 g. of fresh liver. Dose.—3 to 5 tablespoonfuls daily. **Hepatopson pro injectione**, for intramuscular injection, 2 ml. = 600 g. of fresh liver *per os*. Dose—In grave cases, 6 to 8 ml. daily, in slight cases 2 to 4 ml. daily or 5 to 10 ml. at intervals. **Hepatopson "forte"** for intramuscular injection, 2 ml. = 5000 g. of fresh liver *per os*. Dose.—2 ml., increased up to 4 or 6 ml. in grave cases.

**Hepol** (Allen & Hanburys, London) Concentrated liver extract. Issued in both dry and liquid forms for oral use, and as elixir and capsules also in ampoules for intramuscular and intravenous injection.

**Inhepton** (Merck, Darmstadt; Martindale, London) A liver extract for intramuscular injection.

**Lextron** (*Lilly, London*) Capsules contain liver-stomach concentrate 0.433 g., green iron and ammonium citrate 0.2 g., vitamin B complex (adsorbed) 0.016 g. *Dose*—3 or more capsules thrice daily (9 capsules produce 75% as much hæmoglobin as 300 g. of fresh liver)

**Liver Extract Fraction A5** (*Sharpe & Dohme, London*) A dry liver extract of which 1 g. = 20 g. of fresh liver

**Liveroid** (*Oxo, London*) Liquid extract of liver

**Livogen** (*British Drug Houses, London*) Liquid liver extract, hæmoglobin and vitamin B. A tonic in all anæmic conditions

**Livron** (*Boots, Nottingham*). Compound extract of liver, malt, iron and yeast (1 oz. contains 90 gr. of iron and ammonium citrate) *Dose*—1 tablespoonful twice daily. In secondary anæmias and as a general tonic.

**Neoboviline 20** (*Petrolagar Laboratories, London*) Organic compound of liver extract and beef blood, 1 dr. = 0.83 oz. of fresh liver *Dose*—1 tablespoonful four times daily. Reconstructive tonic.

**Parenamaps** (*Paines & Byrne, London*) Liver extract for intramuscular injection, 2 ml. = clinical equivalent of 600 g. of fresh liver **Parenamaps Forte** 2 ml. = clinical equivalent of 5000 g. of fresh liver

**Perhepar** (*Richter, London*) Liver extract. 1 g. or 10 ml. = 100 g. of fresh liver. Supplied in tablets and ampoules

**Pernæmon** (*Organon Laboratories, London*) Protein-free fraction of mammalian liver containing the anti-anæmic principle prepared for intramuscular injection. 1 ml. representing 5 g. of fresh liver, when given by injection, is equivalent to 500 g. of fresh liver. It is also prepared for oral administration.

**Pernæmon Forte**. Concentrated form of Pernæmon giving stable colourless solution. 32 to 64 mg. gives maximal response

**Trephonyl** (*Benguel, London*). Fetal liver extract, horse serum and embryonic juice *Dose*—10 to 20 ml. daily *per os*. In all types of anæmia and in convalescence

**Xorox** (*Napp, London*) Hæmotonic prepared from liver, spleen, stomach and anterior pituitary *Dose*—In adults, 2 tablets thrice daily, smaller doses in children. In anæmia and debility and for backward children

### Hæmopoietic Principle in Liver.

The concentration of the active principle was carried a stage further by the work of Dakin and West (*J. biol. Chem.*, 1935, 109, 480). Starting with Cohn's "Fraction G" a yield of 1% of a highly potent product was obtained. The method adopted involved a complex series of precipitations in which, after removal of inert material with calcium acetate in alcoholic solution, the active principle was precipitated with Reinecke salt (ammonium tetrathiocyanatodiammino-chromium,  $\text{NH}_4[\text{Cr}(\text{NH}_3)_2(\text{SCN})_4]\cdot\text{H}_2\text{O}$ ), regenerated by means of dimethylaniline and amyl alcohol and further purified by repeated precipitation with ammonium sulphate and magnesium sulphate. To this product the name **Anahæmin** has been given. It is a light buff-coloured granular powder, soluble in water and dilute alcohol, but insoluble in dehydrated alcohol and in ether. On hydrolysis it yields an aminohexose and a number of amino-acids. Pyrimidine or purine bases are absent. The substance is slowly decomposed by pepsin and more rapidly by erepsin and alkalis. Pancreatic juice has no effect upon it. 30 mg. on injection gave a perceptible reticulocyte response and 80 mg. gave a maximum response.

The results in 36 cases of pernicious anæmia indicate that anahæmin is highly active for blood regeneration. Total quantities of 1 to 6 ml. (100 to 600 mg., average amount 359 mg.) administered, usually in divided doses, to 11 cases with initial red blood cell counts below 2 millions per c.mm. were sufficient to cause an average increase of erythrocyte concentration amounting to 2.31 millions in



40 days. Good responses followed the administration of amounts sometimes as small as 10 mg. daily or 100 to 200 mg. as a single dose. For maximal reticulocyte responses and for the production of red blood cells at a maximal rate, larger doses were usually required. There is not sufficient data to assess quantitatively the potency of anahæmin as compared with other liver extracts, but no other liver extract given in the small amounts used in the investigation produced such striking results. Preliminary observations suggest that this highly purified fraction may prove to be at least as potent as other liver extracts in the treatment of neurological manifestations of pernicious anæmia.—C. C. Ungley, L. S. P. Davidson and E. J. Wayne, *Lancet*, i/1936, 349.

The fractionation of liver extracts containing the anti-pernicious anæmia principle by means of Reinecke acid to yield a more highly potent fraction has been confirmed. Using this method products have been obtained of which 58 mg. produced a maximal reticulocyte response and a rapid remission in a patient with pernicious anæmia. Applying this method to other methods of separation a further increase in hæmopoietic potency has been secured so that as little as 18 mg. of the product has been sufficient to initiate a maximal reticulocyte response and rapid remissions in pernicious anæmia.—J. F. Wilkinson, *Lancet*, i/1936, 354.

Chemical nature of hæmopoietic substances present in liver—*J. Amer. med. Ass.*, ii/1935, 204.

**Anahæmin B.D.H.** (*British Drug Houses, London*). The active hæmopoietic principle of liver of Dakin and West. *Dose*.—2 ml. (200 mg.) injected monthly is an adequate dose for average cases, though in severe cases up to 4 ml. may be necessary.

### **Stomach Tissue.**

Acting on the suggestion of Castle (*Proc. R. Soc. Med.*, ii/1929, 58) that the stomach secretes a factor which reacts with meat to give a principle which is effective in pernicious anæmia, a desiccated preparation of whole stomach from the pig, freed from fat, of which 30 g. was equivalent to 218 g. of fresh stomach, was tested clinically by Sturgis and Isaacs (*J. Amer. med. Ass.*, ii/1929, 747) and found effective in doses of 15 to 30 g. daily, the activity being equivalent to that of an active liver extract representing 300 to 600 g. of fresh liver.

**Ventriculus Desiccatus (B.P.C.).** *Syn. and Prop. Names* DESICCATED STOMACH, ERYTHROID (*Oxo, London*), EUGASTROL (*Allen & Hanburys, London*), EXTOMAK (*Benger, Manchester*), GASTER SICCATA (*British Drug Houses, London*), GASTREXO (*Evans, Sons, Lescher & Webb, Liverpool*), PEPSAC (*Boots, Nottingham*), VENTREMON (*Organon Laboratories, London*), VENTRICULIN (*Parke, Davis, London*).

*Dose*— $\frac{1}{2}$  to 1 oz. (8 to 30 g.).

The initial dose of desiccated stomach should not be less than 1 oz. and this dose should be maintained till blood count has returned to normal or till the nervous symptoms have gone, when it may be reduced gradually, but it is wise to maintain a small regular dose indefinitely.—J. F. Wilkinson, *Practitioner*, ii/1933, 413.

The fresh whole stomach of the pig, freed from extraneous fat, dried below 40° and ground; the dried material is defatted, dried without heat and ground to a coarse powder.

The activity of stomach preparations is destroyed by heating for one hour to 70°; desiccation is usually carried out below 45°, and the material should not be heated before administration to the patient.—R. West, *J. Amer. med. Ass.*, ii/1935, 432.

**PERNICIOUS ANÆMIA** Sturgis and co-workers, *J Amer med Ass.*, 11/1929, 93; J. Wilkinson, *Brit. med. J.*, 1/1930, 236, A. Renshaw, *ibid.*, 1/1930, 334, Castle and Locke, *ibid.*, 1/1929, 1120; Résumé, *Brit. med. J.*, 11/1930, 437, C. E. Stokes, *Brit. med. J.*, 11/1930, 582, G. T. Allerton, *Lancet*, 11/1930, 795.

Desiccated hog stomach (30 g. = 190 g. of fresh tissue) and hog stomach defatted with petroleum benzine (30 g. = 218 g. fresh tissue) produce satisfactory remission. 15 to 30 g. equal in effect to 300 to 600 g. fresh liver — E. A. Sharpe, *J Amer. med Ass.*, 11/1929, 749.

Undoubtedly better than liver. Erythrocytes and hæmoglobin increased 157% and 94% respectively, compared with 90% and 77% respectively with liver. Hydrochloric acid and pepsin do not appear to be necessary for relief of symptoms — J. F. Wilkinson, *Brit med J.*, 1/1931, 85. See also C. S. Don and C. E. Jenkins, *ibid.*, 158.

Hog stomach better than ox or sheep. Interesting account of long treatment of a case with large amounts. Normal initial dose in a severe case need not exceed 1 to 1½ oz. daily — J. F. Wilkinson, *Brit med. J.*, 1/1931, 585.

A highly potent extract is obtained by incubating Cohn's "Fraction G" with stomach tissue. 6 g. daily is a sufficient dose. — G. B. Walden and G. H. A. Clowes, *Proc Soc exp. Biol, N Y.*, 1/1932, 873.

Only tissue from the pyloric end of the stomach is effective — E. Meulengracht, *Proc. R. Soc. Med.*, 1/1935, 841.

The development of remedies for the treatment of pernicious anæmia—general discussion with bibliography — W. B. Castle, *Amer J Pharm.*, 1936, 55.

**PELLAGRA** treated with desiccated stomach tissues — T. D. Spies, *J Amer med Ass.*, 1/1935, 1377.

**Extralin** (Lilly, London) Liver extract which has been incubated with stomach tissue, capsules contain 0.5 g. Maintenance dose in pernicious anæmia, 3 or 4 capsules thrice daily.

**Hogastrin** (Giles, Schacht, Bristol) A liquid extract of hog stomach.

Dose — 1 to 2 dr.

**Hoggex** (Paines & Byrne, London) Concentrated preparations of hog stomach. Available in powder, capsules, ampoules and solution. Dose (of powder) — ½ to 1 oz. daily, up to 2 oz. in subacute combined degeneration. Maintenance dose, about 5 g. daily. Capsules (5 g.), ampoules (5 g. in 2 ml.) and solution 1 oz. are each equivalent to 80 g. of fresh stomach.

### The Hæmopoietic Factor in Desiccated Stomach.

Castle (*Amer. J. med. Sci.*, 11/1929, 748; *ibid.*, 11/1930, 305, *Lancet*, 1/1930, 1062) showed that gastric digestion liberates anti-anæmic principles from certain foodstuffs which before digestion have no anti-anæmic properties. He regards the anti-anæmic principle as something derived from the interaction of an intrinsic factor contained in gastric juice and an extrinsic factor contained in certain foods, the product being stored in the liver. The intrinsic factor, lack of which causes Addison's anæmia, is thermolabile, being completely inactivated at 70°.

The view has been advanced that the extrinsic factor might be vitamin B<sub>12</sub>—but this is now considered unlikely since several workers have failed to produce improvement in pernicious anæmia patients by administering gastric juice with various sources of vitamin B<sub>12</sub>. It is probable that in those anæmias cured by suitable diets, the intrinsic factor is produced by the stomach, but the extrinsic factor is missing from the food, whereas in typical pernicious anæmia it is the intrinsic factor which is absent.

The following references deal with the nature of the extrinsic factor.

The extrinsic factor is not present in casein, gluten, nucleo-protein from hen's blood, nucleic acid of animal origin or of yeast. Moderate amounts are

present in washed beef muscle protein, large amounts in spleen pulp and autolysed yeast. It is closely allied to vitamin B<sub>12</sub> if not vitamin B<sub>12</sub> itself.—M B Strauss and W. B. Castle, *Lancet*, 11/1932, 111

The filtrate obtained after precipitating the bulk of the protein in Marmite with 80% alcohol still contains the extrinsic factor. Since 80% alcohol destroys or inactivates the vitamin B<sub>12</sub> in watery extracts of yeast (H Chick and A M Copping, *Biochem. J.*, 1930, 1744) it was concluded that vitamin B<sub>12</sub> is not the extrinsic factor. Again, an extract of egg-white, which contains vitamin B<sub>12</sub>, was completely inactive, even in doses equivalent in vitamin B<sub>12</sub> content to more than seven times the curative dose of Marmite. Further, yeast itself and aqueous extracts of yeast of known vitamin B<sub>12</sub> potency were inactive, but Marmite, after severe heating in alkaline solution and containing, therefore, at most, only traces of the vitamin, retained some curative power. Preparations containing vitamins B<sub>1</sub>, B<sub>2</sub> and B<sub>6</sub> had no hæmopoietic properties in tropical macrocytic anæmias. Marmite was actively curative in similar cases, and the hæmopoietic factor was soluble in water and alcohol 80%, and was heat stable.—L. Wills, *Lancet*, 1/1933, 1283, also L. Wills and A. Naish, *Lancet*, 1/1933, 1286

The egg extract used by Wills (see above) was not rich in vitamin B<sub>12</sub>. A definite reticulocyte response obtained from 100 g of egg white predigested with gastric juice.—D K. Miller and C R. Rhoads, *New Engl J Med*, 1/1934, 921.

Two cases of macrocytic hyperchromic anæmia associated with tetany and steatorrhœa in which the anæmia was cured by Marmite—J. Vaughan and D. Hunter, *Lancet*, 1/1932, 829

No parallelism between vitamin B<sub>12</sub> potency and hæmopoietic effect in pernicious anæmia.—C C. Ungley and G V. James, *Quart J Med.*, 1934, 523

Pepsin is antagonistic to the anti-pernicious anæmia factor in stomach (Castle's "intrinsic factor"). In pernicious anæmia the feeding of (a) pepsinised Ventricle was ineffective, (b) depepsinised gastric mucosa, without the addition of beef, was effective, (c) depepsinised gastric mucosa, incubated with dilute hydrochloric acid, without the addition of beef, was effective, (d) depepsinised gastric mucosa, incubated with dilute hydrochloric acid and pepsin, was ineffective, (e) normal gastric juice, peptically inactivated, was effective without the addition of beef or other source of "extrinsic factor". These experiments speak against the existence of "extrinsic factor" as conceived by Castle, and his basic experiments may now be explained by a mechanism which excludes the action of the so-called extrinsic factor. This is based on the demonstrated antagonism of pepsin towards the anti-pernicious anæmia factor and also on the known adsorptive capacity of protein for pepsin. A new method for making oral and injectable stomach preparations is available in which the antagonistic action of pepsin is removed.—E A. Greenspon, *J Amer med Ass*, 1/1936, 270

The above conclusions are criticised on the basis of experimental data obtained in 14 cases of pernicious anæmia. A watery extract of fundus mucosa of pigs' stomachs (pH 8.0 to 8.5), containing pepsinogen but prepared in a manner designed to prevent activation of pepsin when administered, together with a source of extrinsic factor, gave results in 2 cases and a negative but inconclusive result in a third. A concentrate of pure pepsinogen in glycerin was likewise ineffective as a source of intrinsic factor in 1 case. A watery extract (pH 8.0 to 8.5) of pylorus mucosa, prepared as for fundus, when administered in amounts derived from 40 grammes of mucosa, together with a source of extrinsic factor, was effective in 6 cases. The intrinsic factor was not destroyed by a degree of alkalinity (pH 9.8 for 30 minutes) which will inactivate pepsin and pepsinogen (2 cases). Pepsinogen and the anti-anæmic factor are dissociated physiologically and anatomically in the stomach. Depepsinised gastric juice and pepsin-free extracts of pylorus mucosa had little or no hæmopoietic effect when given orally unless interaction with a source of extrinsic factor (e.g., autolysed yeast) was allowed. In these circumstances the rôle of the extrinsic factor could not be attributed to adsorption of pepsin, since none was present. The effect of intrinsic and extrinsic factors given simultaneously is considerably greater than the sum of effects, if any, produced by the two factors given under conditions designed to prevent their interaction. This interaction of intrinsic and extrinsic factor does not require incubation outside the body. Since autolysed yeast in the dose employed (12 g daily) required interaction with normal gastric juice or pylorus extract to render it effective for blood regeneration, it probably acts by virtue of its content of extrinsic factor and not because "it contains elements that are capable of stimulating the cells that elaborate the gastric anti-anæmic agent or because these elements furnish material for

the synthesis of the latter." None of the findings in this investigation was incompatible with Castle's basic hypothesis —C. C. Ungley and R. Moffett, *Lancet*, 1/1936, 1233

Various clinically tested preparations of stomach and liver examined for their content of iron and copper showed no obvious relationship between the content of these metals and hæmatopoietic properties —Jackson, Klein and Wilkinson, *Biochem J*, 1935, 330

The active principles in liver and in hog stomach effective in pernicious anæmia are not identical. The active principle of liver is either a nitrogenous base or a polypeptide, while that of hog stomach is of an enzyme-like nature ("hæmopoietin") —J. F. Wilkinson and L. Klein, *Lancet*, 1/1932, 720.

Hæmopoietin is much more stable than, and has different properties from, the active anti-anæmic principle in liver. Evidence indicates that it is of an enzyme nature and it is extremely sensitive towards heat and chemical treatment. It is present in the normal stomachs of man, carnivorous animals and omnivorous animals, but not in herbivorous animals. It is considered that the enzyme, hæmopoietin, by acting on some substance present in protein food, e.g., beef, may produce *in vivo* a substance which is stored as the active principle found in liver until it is required for red cell formation. The available evidence goes to show that true pernicious anæmia is a type of deficiency disease characterised by the absence from the gastric secretion of a specific enzyme (hæmopoietin), in addition to the pepsin and hydrochloric acid —J. F. Wilkinson and L. Klein, *Lancet*, 11/1933, 632.

A thermo-stable hæmatopoietically active substance prepared by action of hæmopoietin on beef, similar to anti-anæmic principle of liver —Klein and Wilkinson, *Biochem J*, 1934, 1584

**ADDISIN** A substance present in the normal gastric juice of man, destroyed by boiling, dialysable through collodion and exhaustible withstands chemical treatment known to destroy enzymes. It has been found in the gastric juice of swine, dogs and cattle, and is believed to be widely distributed in the animal kingdom. One injection of 4 ml of swine juice concentrated to a volume of 1 to 5%, given intramuscularly in a case of pernicious anæmia, resulted in 4 months in an increase of red blood cells from 1.6 to 4.5 millions, and of hæmoglobin from 50 to 91%. Indications are that addisin is the physiological hormone responsible for the normal state of the blood in health —R. S. Morris and co-workers, *Brit med J*, 11/1932, 1050

J. F. Wilkinson questions these results and is of the opinion that the active substance is in the nature of an enzyme or similar thermolabile substance —*Brit med J*, 11/1932, 1163

**Duodeni Membranam (B.P.C.)** *Syn* PULVIS DUODENALIS, DUODENAL POWDER. *Dose* —3 to 10 grains (0.2 to 0.6 g.)

A greyish-brown hygroscopic powder containing one-fifth its weight of calcium phosphate. It is obtained from the upper portion of the duodenum of the pig, the mucous membrane being scraped off, scaled and powdered. It contains secretin, enterokinase, erepsin, invertase, lactase and maltase. Its therapeutic use is based on the presence of enterokinase which produces trypsin from the trypsinogen of pancreatic juice.

### Liquor Duodenalis.

A protein-free solution of the active constituents of duodenal membrane representing 10% of fresh duodenal mucous membrane. The solution is stable only if acid, sterile and stored in the dark. Has been administered by injection as a stimulant to the production of the external secretion of the pancreas, and slightly increases the secretion of bile.

**Secretin.** Extracted from the duodenal membrane with alcohol, sodium chloride or 0.4% hydrochloric acid, and nearly neutralising whilst boiling to precipitate proteins. The secretin will be left in the filtrate. It is soluble in water and alcohol. Secretin preparations are inactive *per os* since it is destroyed by pepsin and trypsin. Is usually administered as Liquor Duodenalis.

**Secretogen Elixir** (*G. W. Carnrick, Newark, N.J.; Brooks & Warburton, London*). A preparation of secretin intended to replace pepsin and acid mixtures as indigestion remedy. It is stated to contain pyloric prosecretin (with  $\frac{1}{100}$  % of hydrochloric acid to change it to secretin) and duodenal secretin. *Dose*.—1 to 2 drachms. Secretogen Tablets (5 gr.) containing the duodenal and pancreatic secretins are suggested particularly in faulty digestion of starch, with fermentation and flatulence.

**Mucin.** *Dose*.—5 to 10 grains (0.3 to 0.6 g.).

This is the essential constituent of the secretions of mucous membranes (buccal, nasal, pharyngeal, etc.). It is precipitated from these by alcohol and by acetic acid. The saliva produced by the submaxillary and sublingual glands contains it, but not the parotid. It may be procured from areolar or connective tissue, and from bile.

Taken internally, *e.g.*, in tablets containing mucin 5 gr., with sodium bicarbonate 5 gr., relieves painful digestion, gastritis and gastric ulcer. In the form of a spray containing mucin 5 gr., sodium bicarbonate 5 gr., menthol 1 gr., lime water  $\frac{1}{2}$  oz., distilled water  $\frac{1}{2}$  oz., has been found of value in dry catarrhs, rhinitis, etc., pharyngitis, and where incrustations are present on the laryngeal lining.

Superior to all other treatment in many throat and stomach complaints, *e.g.*, gastric ulcer. Powdered hog's stomach possibly only acts by virtue of the mucin contained.—W. Stuart-Low, *Brit. med. J.*, ii/1931, 124.

Results from gastric mucin in doses of from 90 to 100 g. daily indicate considerable promise from this form of therapy. Gastric mucin is a very viscid unpalatable preparation, and the taste is somewhat difficult to disguise.—Preliminary report of Council on Pharmacy and Chemistry, *J. Amer. med. Ass.*, i/1934, 767.

Gastric mucin has been employed in the treatment of peptic ulcers. It probably exerts a protective action by virtue of its viscous nature and of its buffer action. Symptomatic relief reported in from 63 to 93% of cases studied.—K. A. Martin, *J. Amer. med. Ass.*, i/1936, 1468.

**Biomucine** (*Robert et Carrière, Paris, Anglo-French Drug Co., London*)

Natural mucin of the gastric mucosa, free from histamine. Supplied in cachets for treatment of hyperchlorhydria, gastric ulcer or duodenal ulcer.

**Enteromucine** (*Robert et Carrière, Paris, Anglo-French Drug Co., London*)

Natural mucin of the intestinal mucosa, in granules for oral use in constipation, or in powder form for douches (2 teaspoonfuls in 250 ml. of water) in the treatment of recto-colitis, sigmoiditis, etc.

### Spleen Substance Desiccated.

*Dose*.—5 to 10 grains (0.3 to 0.6 g.). 1 part represents 5 of the fresh spleen. Has been used in anæmia, tuberculosis, myxœdema, etc. Value in typhoid and malaria possibly due to splenic hormones.

Extract of pig's spleen stated to give 100% of recoveries in tuberculosis of first degree and 75% in all—several hundred cases treated since 1903. One or two injections of 5 ml. intramuscularly (thigh) or subcutaneously (abdomen) daily for adults. Oral route (in syrup) for prophylaxis, or adjuvant to injections; 4 tablespoonfuls given daily with meals to adults, representing 25 g. spleen tissue. *Dose* injected, or *per os*, proportionally less for children. Treatment absolutely harmless.—Bayle, *per J. Amer. med. Ass.*, ii/1925, 1434.

Calcium metabolism stimulated by spleen, preparing suitable calcium salts for the blood stream and body cells. Splenic and

parathyroid extracts suggested for treatment of pulmonary tuberculosis.—per *Prescriber*, 1926, 227.

**Diglobin** (*Anglo-French Drug Co, London*). Total extracts of spleen and epiphyseal bone marrow in tablets containing 0.3 g. *Dose*.—2 tablets thrice daily before meals. In anaemia and chlorosis.

**Neo-Hormonal** (*Schering, London*). An extract prepared from the spleen containing the hormone which stimulates intestinal peristalsis. *Dose*.—In chronic constipation, 35 ml. intravenously and then 5 ml. intramuscularly, in post-operative intestinal paralysis, 20 ml. intravenously or intramuscularly, repeated if necessary intravenously after 5 or 6 hours. (The intramuscular injection contains 0.16% of benzamine.)

**Splenex** (*Plasmon, London*). A liquid extract of spleen substance (4 oz. = 2½ lbs. raw spleen), sweetened and flavoured. *Dose*.—½ to 1 tablespoonful daily for 3 weeks, with a week's interval between courses.

**Splenoxoid** (*Oxo, London*). Liquid extract of spleen. Treatment of tuberculosis of lungs, bones, and joints, and of polycythemia.

### Extracts of Muscle and Other Tissues.

Several preparations stated to cause vasodilatation have been suggested for use in the treatment of hypertension, angina pectoris and intermittent claudication. The substances employed for this purpose include extracts from striated muscle, liver, kidney, pancreas and urine. The nature of the active principles in these actions is still a matter of controversy.

According to Frey (1926) there is excreted in the urine a substance which has a pronounced effect on the cardiac rate and amplitude, and on the flow of blood through the coronary vessels. This substance is believed by Frey to be derived from certain tissues, especially the pancreas, and to be a specific "cardiac hormone." It is present in the blood, but in an inactive form which can easily be converted into the active form. It is present in smaller amounts in extracts of other tissues. When the pancreas is removed the amount of cardiac hormone excreted in the urine is reduced to about 20% of the amount normally excreted. Haberlandt in 1924 showed the presence in heart muscle of a substance which had a stimulating effect on the heart beat, and Schwartzman showed that extracts of skeletal muscle have a similar effect.

Extract of heart muscle in angina pectoris and intermittent claudication — M. S. Schwartzman, *Brit. med. J.*, 1/1930, 855, *ibid.*, 1/1931, 493.

Intermittent claudication well treated by Lacarnol and Padutin — M. Newman, *Brit. med. J.*, 1/1933, 611. See also *Brit. med. J. Epit.*, 1/1931, 82.

All have essentially similar action, none can replace digitalis in myocardial weakness or cardiac irregularity. Use not entirely without risk and caution necessary. Precise use and limitations still to be determined — *Lancet*, 1/1931, 28.

Frey's hormone injected into the jugular vein produces a quick and sharp fall in systemic blood volume. At the same time it increases the relative coronary outflow. The effects of muscle extract are very similar to those of pancreatic tissue extract, but more pronounced — C. W. Greene, *J. Pharmacol.*, 1936, 57, 98.

**Animass** (*Organotherapeutic Labs, Osnabrück, Braun, London*). An organic product derived from intima and media of young cattle, foetal extract and by-products of erythrocytes. For use in arteriosclerosis. In tablets, and ampoules for intramuscular injection.

[P1-81-84] **Angiolysin** (*Coates & Cooper, London*). Tablets contain adenosine-phosphoric acid 0.0012 g. and pyrrhodid (amidopyrine-rhodan compound) 0.125 g. In angina pectoris.

**Angioxyl** (*Laboratoires des Proxystases, Paris; Bengué, London*). An insulin-free extract of pancreas for treatment of hypertension. In 2 ml. ampoules for intramuscular injection, 1 to 4 times daily; also as a syrup for oral administration, 2 ml. being equivalent to 12 g. of fresh gland

**Carnacton** (*Cavendish Chemical Co., London*) Diaphragmatic muscle extract. *Dose*—From 1 ml. per day to 2 ml. several times daily hypodermically or intramuscularly, or 25 to 40 drops of solution *per os* from once to several times daily

**Cardone** (*Paines & Byrne, London*) Muscle extract from heart and skeletal muscle, and also from the liver and pancreas. *Dose*—10 to 25 drops on a lump of sugar 1 to 3 times daily before meals, or 1 ml. once or twice daily intramuscularly. Angina pectoris, vascular disease, etc

**Eutonon** (*Promonta, Hamburg, Pharmaceutical Products, London*) Vaso-dilator substance obtained from the liver for use in angina pectoris and intermittent claudication. *Dose*—1 or 2 ml. intramuscularly once or twice daily, intermediate and after-treatment 20 to 30 drops of Eutonon Liquid thrice daily

**Lacarnol** (*Bayer Products, London*) A nucleoside preparation from organic tissues. *Dose*—10 to 25 drops *per os* 1 or 3 times daily, 1 ml. once or twice daily subcutaneously or intramuscularly. In angina pectoris and allied vascular diseases when due to arteriospasm.

**M.A.P.** (*Henning, Berlin; Pharmaceutical Products, London*) Muscle adenosine-phosphoric acid, the active principle of muscle extract. *Dose*—1 or 2 ml. intramuscularly from 1 to 3 times daily, or 1 or 2 ml. (= 10 or 20 mg.) intravenously for heart failure only. For heart failure, angina pectoris and other cardiovascular diseases

**Myoston** (*Henning, Berlin, Pharmaceutical Products, London*) Extract of skeletal muscle with a standardised content of 0.25 mg. muscle-adenosine-phosphoric acid in 1 ml. *Dose*—1 ml. subcutaneously or intramuscularly once or twice daily, or 20 drops *per os* 3 or 4 times daily. Indications as for M.A.P., and especially in the protracted treatment of angina pectoris

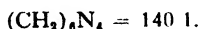
**Padutin** (*Bayer Products, London*) Preparation of a vasomotor hormone obtained from pancreas. For oral or intramuscular use in angiospasm, Raynaud's disease, and generally for regulating blood pressure

**Telatuten** (*Lustpold-Werk, München, Medical Laboratories, London*) Physiological active principle of the wall tissues of animal blood vessels. Intravenously in arteriosclerosis, angina pectoris, etc., and *per os* in pulmonary emphysema and chronic bronchitis

**Vagotonine** (*Byla, Paris, Anglo-French Drug. Co., London*) Preparation of a pancreatic hormone. *Dose*—0.02 g. subcutaneously. For arterial hypertension and paroxysmal tachycardia

## HEXAMINA

B.P



*Syn. and Prop. Names.* HEXAMETHYLENETETRAMIN (*P.G. VI*), HEXAMETHYLENAMINA (*P. Helv. V, P. Dan., P. Ned. V, P. Jap., Fr. Cx. Supp. 1920, F.E. VIII, P. Belg. IV, P. Ital. V*), METHENAMINA (*U.S.P. XI*), UROTROPINE, AMINOFORM, FORMIN, FORMAMINE, URISOL, METRAMINE (*Oppenheimer, London*), URITONE, VESALVINE (*Martindale, London*).

The trade-mark "Urotropine," No. 215652, was "avoided" in Gt. Britain by order of the Board of Trade

*Dose.*—10 to 30 grains (0.6 to 2 g.) in a large volume of water. Very large doses may be given in conjunction with alkalis when not administered for urinary infections (*vide infra*). *U.S.P. XI* average dose 5 grains.

*P. Ned.* V max. single dose 1 g; max daily dose 4 g For children, 3 to 4 grains in water to 5 times during the day.

**Intravenously**—75 minims (5 ml) of 40% solution. Larger doses have been given

Colourless crystals, sublimable.

**Soluble** 1 in  $1\frac{1}{2}$  of water giving alkaline solution, 1 in 8 of alcohol 90%; almost insoluble in ether

It burns with intense heat and without soot. A 5-grain tablet will boil a test tube half-full of water.

**Pharmacology.** Although the amount of formaldehyde liberated from therapeutic doses of hexamine cannot be sufficient to kill *B. coli*, the slow generation of formaldehyde by the drug in the presence of acid inhibits bacterial growth. It is preferable therefore to raise the acid index of the urine within reasonable limits.

Hair, Lepper and Martland found the greatest concentration of HCHO in the urine, after giving hexamine, was 1 in 20,000, whereas anything less than 1 in 5000 is said not to be bactericidal. They found that only when the pH of the urine had fallen to 4 are effective doses of HCHO liberated. The urine should be collected under toluene and the pH tested with phenol red.—D. Navarro, *Brit. med. J.*, 11/1930, 417.

**Uses.** Disinfectant in cystitis and urinary infections. The pyuria of tabes dorsalis, cholelithiasis and gonorrhœa (early stages) have been well treated

As a urinary antiseptic, hexamine decomposes, liberating formaldehyde more readily in presence of acid, hence the administration of sodium acid phosphate is advised. It may be well to give the latter 1 or 2 hours before the hexamine.

**ACIDOSIS, NON-DIABETIC.** Due to infection with *B. coli*, well treated by intravenous injections.—J. Fraser, *Brit. med. J.*, 1/1924, 571.

**CHOLECYSTITIS.** It has been shown by Knott that bile obtained through a duodenal tube, after the administration of large doses of hexamine, is strongly antiseptic, although alkaline. Formerly the maximum dose of hexamine which could be given with safety was limited by the supposed necessity for keeping the urine acid, but just as efficient an action as a biliary antiseptic can be obtained when sufficient alkali is given to prevent the formation of formaldehyde. Under such conditions enormous doses of hexamine can be given without causing any bladder irritation. A mixture containing 60 gr. each of sodium bicarbonate and sodium citrate is given after breakfast, after tea and the last thing at night after drinking a glass of milk or water. The reaction of the urine is tested every time it is passed, as soon as it is found to be constantly alkaline, if necessary after the dose of alkalis has been increased, 100 gr. of hexamine is added to the mixture, so that 300 gr. is given daily. The treatment can be continued for six weeks. The hexamine sterilises the bile ducts and gall-bladder, and when combined with non-surgical biliary drainage by means of Epsom salts, it results in the cure of most cases of cholecystitis.

This treatment should be given for a week or two before and after operations on the gall-bladder and bile ducts in order to guard against septic complications. In severe infective cholangitis with jaundice, high temperature and rigors, it has appeared to save life.

Large doses in the manner just described are also worth trying in the acute stages of encephalitis and in the cerebral complications of ear and sinus disease and for contacts in poliomyelitis epidemics.

Doses of 15 to 30 gr., although official, if given alone or with sodium acid phosphate, are liable to cause hæmorrhagic cystitis.—A. F. Hurst, *Pharm. J.*, 11/1934, 676.

Hæmaturia caused in a case of acute encephalitis due to hexamine in doses of 20 gr. every 6 hours.—Sir Thomas Horder, *Brit. med. J.*, 1/1927, 995.

Operations on the biliary tract should be preceded by hexamine 10 grains 3 times a day for a week at least.—W. E. M. Mitchell, *Lancet*, 11/1927, 270.



**CHOREA** in children well treated intravenously. In one case 18 injections, increasing from 2 to 6 ml. of a 5% solution, were made in 6 weeks. More recently 10% solution has been used with good results.—*Per J. Amer. med. Ass.*, 11/1925, 1098. Seems to give best results by intravenous injection when the chorea is associated with an infection, e.g., encephalitis or polyarthritis.—*De Capua, J. Amer. med. Ass.*, 11/1929, 808.

**CYSTITIS.** Many remedies have been introduced and widely advertised as cures for urinary infections, but hexamine remains the most useful of the urinary antiseptics.—*J. Thomson Tait, Brit. med. J.*, 11/1935, 1252.

**EPILEPSY.** A case of 20 years' standing, having 3 to 8 fits a day, which 60 gr of bromide thrice daily failed to control, was cured by treatment with hexamine 10 gr. and ammonium bromide 20 gr. twice daily, with 1 teaspoonful of sodium citrate in water twice daily.—*E. G. McCarthy Morris, Lancet*, 1/1926, 834.

**EYE INFECTIONS.** Considerable success with hexamine and acid phosphate internally in inflammatory conditions of the anterior chamber of the eye.—*M. A. F. Sherf, J. Pharmacol*, Feb., 1930, 237.

**INFLUENZA** and colds treated by 40 to 60 gr. doses every 4 hours with 1 dr doses of sodium bicarbonate.—*J. Geoghegan, Practitioner*, 11/1933, 214.

**MALARIAL COMA** cured in 10 cases by intravenous injection of 3 ml. of 40% solution.—*J. Umansky, Lancet*, 11/1931, 350.

**PYELITIS.** In the acute stages of severe pyelitis 5 ml. of 40% solution intravenously once or twice daily till temperature falls exceedingly effective.—*Hamilton Bailey, Practitioner*, 1/1933, 346.

Hexamine in well acidified urine cures at least one third of the cases of non-surgical pyelitis and cystitis, but there is no method of determining which case will respond.—*D. R. Mitchell and J. M. Scott, Brit. J. Surg.*, 1933, 225.

**PYELITIS OF PREGNANCY.** A single injection of 10 ml. of the solution is often sufficient.—*A. Jacobs, Practitioner*, 11/1927, 219.

**RETENTION OF URINE.** Treated by 5 to 10 ml. of 40% hexamine solution.—*Brit. med. J. Ept.*, 1/1923, 65.

Post-operative anuria. 7 to 10 ml of 40% solution intravenously—procedure uniformly successful.—*Lancet*, 1/1924, 1118.

**SCABIES** severe, well treated. 10 ml. of a 10% solution injected daily for 3 or 4 days, septic lesions being washed with hot water only during period of injections, but course of injections followed up by application of sulphur ointment.—*N. N. Ghosh, Indian med Gaz*, May, 1925, 221.

**TYPHOID.** 20 grains or more 3 times in 24 hours with an equal quantity of sodium citrate and sodium bicarbonate, starting from the beginning of the second week onwards. If cholecystitis appears give 10 20-gr doses with sufficient alkali in 24 hours and apply Antiphlogistine over gall-bladder region.—*A. E. Gow, Lancet*, 1/1930, 96.

**Mistura Hexaminæ (U.C.H.)** No. 1 Hexamine 10 gr., chloroform water to 1 dr. half an hour before food; No. 2 Sodium acid phosphate 30 gr., chloroform water to 1 dr. half an hour after food.

**Tabellæ Hexaminæ (B.P.C.)** contain 5 gr (0.3 g)

**Tabella Hexaminæ Composita (C.X.H.).** Hexamine 4 gr., sodium glycocholate 1 gr., sodium taurocholate 1 gr., sodium salicylate 5 gr. *Dose*—1 or 2 tablets.

**Acitetramin (Richter, London).** Hexamine acid phosphate. *Dose*—1 or 2 8-grain tablets 3 times a day. Urinary antiseptic; contraindicated in tuberculous cystitis.

**Coerulamin (Richter, London)** Hexamine acid phosphate 0.1 g., methylene blue 0.02 g. *Dose*—5 ml intravenously 3 to 6 times weekly or 2 to 3 tablets daily. For pyelitis, nephritis, gonorrhœa, etc.

**Cylotropin (Schering, London).** Ampoules of 5 ml contain 30 gr. of hexamine, 12 gr. of sodium salicylate, and 3 gr. of caffeine sodium salicylate. *Dose*—5 ml. intravenously or intramuscularly daily or on alternate days. In infective urinary conditions.

**Solvurate (Richter, London)** Granules containing in 5 g hexamine 0.4 g., piperazine 0.1 g., lithium carbonate 0.05 g., sodium benzoate 0.05 g. *Dose*— $\frac{1}{2}$  oz. thrice daily. Pyelitis, renal calculus.

**Uraseptine** (*Rogier, Paris, Anglo-French Drug Co., London*) Granules of hexamine and hexamine citrate, with benzoates and diethylenediamine  
*Dose.*—3 to 6 teaspoonfuls daily Urinary antiseptic and in the uric acid diathesis

**Hexamine Benzoate.** *Prop. Name.* VESALVINE "B" (*Martindale, London*).  $(\text{CH}_2)_6\text{N}_4 \cdot \text{C}_6\text{H}_5 \cdot \text{COOH} = 262 \cdot 2$

*Dose.*—5 to 15 grains (0·3 to 1 g.).

Small scaly crystals containing about 53% of the base Made by combining equivalent quantities and crystallising. Soluble 1 in 50 of water and 1 in  $2\frac{1}{2}$  of alcohol 90%

**Uses.** A urinary antiseptic

**Cystazol** (*Allen & Hanburys, London*). Hexamine sodio-benzoate in 10 gr tablets *Dose.*—1 to 3 dissolved in water twice or thrice daily, in bacterial infections of the urinary tract.

**Uro-Hexoids** (*British Drug Houses, London*). Tablets of hexamine and lithium benzoate. *Dose*—1 or 2 after each meal, taken whole or crushed and dissolved in water Urinary antiseptic, diuretic and anti-lithic

**Hexamine Camphorate.** *Prop. Name.* AMPHOTROPIN (*Bayer Products, London*).  $[(\text{CH}_2)_6\text{N}_4]_2 \cdot \text{C}_8\text{H}_{14}(\text{COOH})_2 = 480 \cdot 4$ .

*Dose.*—8 to 12 grains (0·5 to 0·8 g.). Tablets 8 grains (0·5 g.)

A white crystalline powder made by combining in alcohol, chloroform, etc.

**Soluble** in water 1 in 10 with acid reaction. Solutions are hydrolysed to a great extent.

**Uses.** Urinary antiseptic. An alkaline urine is rendered neutral or acid by administration In chronic cystitis, bacilluria, nephritis

**Amphotropin Solution** (*Bayer Products, London*) 40% solution of hexamine camphorate For intravenous injection in urinary affections

**Hexamine Salicylate.**  $(\text{CH}_2)_6\text{N}_4 \cdot \text{C}_6\text{H}_4 \cdot \text{OH} \cdot \text{COOH} = 278 \cdot 2$ .  
*Syn. and Prop. Name* VESALVINE "S" (*Martindale, London*), SALURENE

*Dose.*—5 to 15 grains (0·3 to 1 g.) in water before meals.

Colourless prismatic crystals with agreeable sweetish saline taste, containing approximately 50% of each constituent. Prepared by combining equimolecular proportions.

**Soluble** 2 in 1 of water and 1 in 2 of alcohol A saturated aqueous solution will remain clear for months, whilst vigorous rubbing on the sides of the vessel will cause a deposition of salicylic acid crystals.

**Incompatible** with acids, alkalis, carbonates and salicylates, hence best administered alone. It decomposes on heating in water or alcohol.

**Uses.** A urinary and intestinal antiseptic in cystitis, bacilluria, gastro-intestinal catarrh, colitis, dysentery, diarrhoea, dyspepsia, and all cases beneficially treated by hexamine. It splits up on passing through the system into its two constituents—the salicylic acid enhancing the effect of the hexamine. It does not irritate the bladder like other antiseptics.

**Elizir Vesalvine "S"** (*Martindale, London*) contains 5 gr. per drachm.

**Neohexal** (*Riedel-de Haen, Berlin; Old Strand Chemical Co., London*) Combination of hexamine and sulposalicylic acid in 0·5 g. tablets  
*Dose.*—1 or 2 tablets dissolved in water thrice daily. Affections of the urinary tract

**Hexamine Sodium Acetate.**

$(\text{CH}_2)_6\text{N}_4, 2\text{CH}_3\text{COONa}, 6\text{H}_2\text{O} = 412.3.$

*Dose.*—30 grains (2 g.). A crystalline salt made by evaporating solutions of the components in the above proportions. Contains approx. 34% of hexamine. In gonorrhœa and cystitis.

**Cystopurin Tablets** (*Genatosan, Loughborough*) Contain 1 g of hexamine sodium acetate

**Hexamine Triborate.** *Prop. Name.* BOROVERTIN (*Bayer Products, London*) (*P. Ned. V*)  $(\text{CH}_2)_6\text{N}_4, 3\text{HBO}_2 = 271.9$

*Dose.*—15 to 60 grains (1 to 4 g.) daily.

Crystalline powder containing about 50% of hexamine, made by combination of 1 mol. of hexamine and 3 mols of boric acid Soluble in water 1 in 13. Urinary antiseptic, *e g.*, in gonorrhœal cystitis, pyelitis, renal calculus and tuberculosis of the bladder and kidneys

**Formamol** (*B.P.C.*) *Syn and Prop Name* HEXAMINE ANHYDROMETHYLENECITRATE, HEI MITOL (*Bayer Products, London*)

*Dose.*—8 to 15 grains (0.5 to 1 g.). White crystals soluble 1 in 5 of water, sparingly soluble in alcohol Is similar to hexamine in its action and is used in infections of the genito-urinary tract

**Urodonal** (*Chatelain, Paris, Spencer & Co., London*) A granular effervescent preparation of hexamine For composition see Vol II *Dose*—3 teaspoonfuls during the day Stated to be useful in removing uric acid and allied bodies

**Pyridium** (*Pyridium Corporation, New York, Menley & James, London*) is phenyl-azo-alpha-alpha-diamino-pyridine hydrochloride A red, microcrystalline powder, slightly soluble in water, readily soluble in hot water *Dose*—3 gr 3 times daily In hyperacidity dose should be regulated and given immediately after meals It possesses anti-bacterial action against cocci and *B. coli*, and is eliminated through the genito-urinary tract Is used in gonorrhœal infections, *B. coli* and mixed infections, pyelitis and cystitis Also used locally as antiseptic in the form of a 1% solution, or ointment (10%)

**Contraindications.** Idiosyncrasy towards the compound when given internally is indicated by colic, nausea, headache and vertigo reduced dosage may, however, establish tolerance, but if not discontinue Kidney disease is a contraindication, and it should not be given in severe hepatitis, where excretion is slow, nor in uræmia Use with caution in severe chronic gastro-intestinal disorders The compound should not be used simultaneously with mercurial irrigations

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## HYDRARGYRUM

*B.P., U.S.P. XI, P. Helv V, P. Dan*

Hg = 200.61

[P1] "Mercury, oxides of; nitrates of mercury; mercuric ammonium chlorides; potassio-mercuric iodides, mercuric oxycyanides, mercuric thiocyanate."

[P2] "Mercuric chloride; mercuric iodide; organic compounds of mercury."

[S1] "Mercuric chloride except substances containing less than 1% of mercuric chloride; mercuric iodide except substances containing

less than 2% of mercuric iodide, nitrates of mercury except substances containing less than the equivalent of 3%, weight in weight, of mercury (Hg); potassio-mercuric iodides except substances containing less than the equivalent of 1% of mercuric iodide, organic compounds of mercury except substances containing less than the equivalent of 0.2%, weight in weight, of mercury (Hg)."

[83] "Mercuric chloride—in batteries."

"Mercuric chloride, mercuric iodide, organic compounds of mercury—in dressings on seeds or bulbs "

"Mercury, nitrates of—in ointments containing less than the equivalent of 3%, weight in weight, of mercury (Hg) "

[86, "Mercury, organic compounds of—specify proportion as the proportion of organically-combined mercury (Hg) contained in the preparation "

Dose —  $\frac{1}{2}$  to 3 grains (0.03 to 0.2 g.), by intramuscular injection,  $\frac{1}{2}$  to 1 grain (0.03 to 0.06 g.)

Mercury has a sp. gr. of about 13.5 and a b.p. of about 358°

**Antidotes to Acute Poisoning by Mercurial Salts.** Give raw white of egg in water in unlimited quantities, but remove it from the stomach as soon as possible by emetic or stomach tube, as albuminate of mercury formed is soluble in excess of albumin and sodium chloride. It is now stated by many authorities that medicinal charcoal in suspension is much more efficacious than white of egg, it should be given and quickly removed, as above.

Discussed point as to whether to give antidote or emetic first—probably best to give whichever comes first to hand, but it is important to remember that much white of egg may lessen efficacy of emetic.

Keep patient warm, give brandy,  $\frac{1}{2}$  oz., or aromatic spirit of ammonia,  $\frac{1}{2}$  dr., in water; alkalinising demulcent drinks freely. Saline and 5% dextrose intravenously. Sodium thiosulphate intravenously said to be of doubtful value.

Sodium formaldehyde sulfoxylate said to be most efficient chemical antidote for mercuric chloride. Details of 10 cases treated. Suggested technique: gastric lavage with 5% solution, 200 ml. to be left in the stomach, 10 g. in 100 to 200 ml. of water intravenously slowly over 20 to 30 minutes. Later, after 4 or 6 hours, 5 to 10 g. intravenously repeated.—Rosenthal, *J. Amer. med. Ass.*, 1/1934, 1277.

Sodium formaldehyde sulfoxylate is a powerful reducing agent more stable in the body than sodium thiosulphate and sodium hydrosulphite. Owing to its low toxicity as much as 10 to 15 g. may be given intravenously in 10% solution, 5 to 10% as gastric lavage, leaving 100 to 200 ml. in the stomach, and a 5% solution by enema. Treatment is repeated in severe, acute cases within 4 to 6 hours, and again in 24 hours. In 1 case reported, treatment consisted of 6 intravenous injections over a period of 4 days. In cases of severe poisoning with mercuric chloride, intravenous injection should be accompanied by oral use and enemas to avoid tissue destruction.—W. E. Robertson and V. L. Tuck, per *J. Amer. pharm. Ass.*, 1935, A-343.

Suggested that 10 ml. of 10% solution of sodium hypophosphite with 5 ml. of hydrogen peroxide in a glass of water, administered by mouth, and used for gastric lavage, is a suitable antidote for mercury poisoning.—J. R. Ross and A. Brown, *Canad. publ. Hlth J.*, 1935, 26, 237.

Immediate gastric lavage important, but subsequently of little effect—first lavage should be thorough. Enemas if diarrhoea is absent. Continuous intravenous drip saline useful, but waterlogging must be avoided.—*Lancet*, i/1936, 617.

Therapeutic effects of gastric lavage, alkalis and intravenous saline described—43 out of 46 cases of mercurial poisoning so treated recovered—W. B. Porter and C. E. Simons, *Amer. J. med. Sci.*, 1934, 188, 375.

Massive alkalinisation has given good results in treatment of acute mercuria poisoning during 8 years of trial—Nanu-Muschel, V. Ciocalteu and C. Ciocalteu, *J. Prat.*, Paris, Apr. 16, 1935.

Treatment of poisoning by mercuric chloride. Gastric lavage with saturated solution and colonic irrigation with 5% solution of sodium bicarbonate, internal administration of it in dosage sufficient to keep urine alkaline to litmus, 500 ml of 5% solution intravenously after lavage—*Brit. med. J.*, 1/1935, 400G.

**Uses.** Mercury is used as a purgative, cholagogue and anti-syphilitic.

**Emplastrum Hydrargyri (B.P.C.)** contains about 33% of mercury.

**Hydrargyrum cum Creta (B.P.)** *Syn.* GREY POWDER

*Dose.*—1 to 5 grains (0.06 to 0.3 g.)

Contains 33% of mercury. Liable to oxidise in the air.

**Hydrargyrum cum Creta (U.S.P. XI)**

*Average dose.*—Laxative, 4 grains (0.25 g.) Mercury, honey and little water shaken together for 10 hours or longer if necessary, chalk made in paste with water, and two parts then mixed and dried, first between bibulous paper and then in a dish at ordinary temperature.

**Injectio Hydrargyri (B.P.)** *Syn.* MERCURIAL CREAM

*Dose.*—5 to 10 minims (0.3 to 0.6 ml.) by intramuscular injection.

Contains about 10% w/v of mercury with camphor and creosote in wool fat and olive oil. Weekly injections are given into the upper and outer quadrant of the gluteal region.

For combined treatment of syphilis with neoarsphenamine and mercury, see p. 215.

**Toxic Effects.** Malaise, stomatitis, dermatitis, nephritis and, rarely, colitis may occur. Malaise is an indication for a reduction in dosage. Stomatitis is the most common symptom. It may be prevented by oral hygiene and by the use of potassium chlorate lozenges. If necessary, sodium thiosulphate may be injected. Must be given with care to those with kidney disease, owing to the irritant action of mercury.

**Cremor Mercurialis (N.H.)** *Staff Surgeon Adams' Formula*

*Dose.*—5 minims (= 1 grain of mercury) given once a week. Mercury 20, wool fat 30, chlorbutol 2, all by weight, liquid paraffin to 100 by measure.

**Injectio Hydrargyri Fortis (B.P.C.).** *Syn.* OLEUM CINEREUM, GREY OIL.

*Dose.*—1 to 2 minims (by intramuscular injection). Contains 40% w/v of mercury.

**Hulle Grise (Fr. Cx.).** Mercury 40, wool fat 26, vaseline oil (*Fr. Cx.*) 60, all by weight. Measures 100, i.e., 40% w/v of mercury. *P. Ned. V* and *P. Belg. IV* are similar. *F.E. VIII* is made with chloroform and contains castor oil, with guaiacol and camphor as preservatives.

**Suppositories** containing the 40% grey oil in various strengths have been used in syphilis. Efficacious, simple and safe.

**Lanolinum Hydrargyri.**

Mercury 100, lanolin (hydrous) 200, mercurial ointment 5, mutton suet 50  
For inunction in syphilis (effect is rapid), used daily 4 to 8 times after a hot bath

**Linimentum Hydrargyri (B.P.C)**

Contains about 30% *w/v* of mercury ointment (equivalent to 9% *w/v* of Hg) with ammonia and liniment of camphor.

Useful stimulant for enlarged joints and glands

**[P2 S1] Massa Hydrargyri (U.S.P. XI) Syn BLUE MASS, BLUE PILL**

*Average dose.*—3 grains (0.2 g.).

Mercury 33, mercury oleate 1, liquorice 10, althea 15, glycerin 9, honey 32. Same strength as mercury pill, *B.P.*

**Pilula Hydrargyri (B.P.) Syn BLUE PILL**

*Dose.*—4 to 8 grains (0.25 to 0.5 g.).

Contains 33% *w/w* of mercury

In raised arterial tension when indicative of danger, a pill twice or thrice weekly, followed by saline, is beneficial.—Brunton

In syphilis, begin with 1½ grains after the first and last meals, increasing the daily dose by 1 grain each week till patient is taking 2 grains thrice daily. An average dose is 2 grains twice a day

In cardiac dropsy it seems to act complementarily to digitalis, and to prove efficient where latter has failed to increase urinary secretion materially. It is to be avoided if renal disease be present. When diuresis is fully established discontinue mercury and give a mixture of caffeine and spirit of nitre with infusion of scoparium

**[P1 S1] Pilulæ Hydrargyri cum Creta et Opii (B.P.C) Syn. HUTCHINSON'S PILLS.**

*Dose.*—1 pill. Contain 1 gr. of grey powder and 1 gr. of Dover's powder (*exempt* [D]). For syphilis; the opium tends to counteract the irritant action of the mercury

**Pilulæ Hydrargyri cum Rheo (B.P.C)**

*Dose.*—1 pill. Contain 2½ gr each of mercury pill and compound rhubarb pill

**Unguentum Hydrargyri (B.P.)**

Mercury, 30% *w/w*, in suet and benzoinated lard. Principally used for inunction in syphilis, also to relieve local inflammation and to destroy pediculi.

*P. Svec.* contains Hydrargyrum Extinctum 36 (*i.e.*, mercury "killed" by rubbing with wool fat, and containing 83.5% of Hg), benzoinated lard 44, suet 20, *i.e.*, about 30% mercury.

The inunction treatment of syphilis should be carried out by a skilled rubber. 5 to 10 g. of ointment should be rubbed for 20 minutes on successive days into thighs, calves, arms, chest and back, a bath being taken on the sixth day and the cycle re-started on the seventh. Number of rubbings varies from 60 to 200 according to patient's tolerance.—L. W. Harrison, *Price's Text-book of Medicine*.

**Absorption of Mercurials from Ointments applied to the Skin.** The method was to rub a weighed quantity into 20 square inches of surface, and ascertain the amount not absorbed. The greatest absorption of mercury took place from a lard basis. Hydrous wool fat was absorbed to a greater extent than lard, but the mercurial was not absorbed with it, so the absorption of mercury was actually less than from a lard ointment of equal strength. Absorption from a paraffin basis was always less than from a lard base. Of the various mercurials examined, mercuric oxide was the most readily absorbed, either as such or in the form of the official oleate, but ointments containing over 10% of the oxide are irritant. Ammoniated mercury and mercury salicylate are absorbed almost as well as the oxide. Mercurous chloride was absorbed to a less extent than any of the mercurials examined. The inunction of 4 g of mercury ointment gave an absorption into the body not exceeding 0.12 g of mercury when used for 2 minutes and 0.17 g in 10 minutes.—R. B. Wild and Ivy Roberts, *Brit med J*, 1/1926, 1076

**Pommade Mercurielle Faible** (*Fr.* (x)) contains 12½% of mercury in benzoinated lard

**Pommade Mercurielle à Parties Égales** (*Fr.* (x)) *Syn* ONGUENT NAPOLITAIN. Mercury 1, benzoinated lard 1

[P281] **Unguentum Hydrargyri Forte** (*U.S.P. XI*) *Syn* STRONG MERCURIAL OINTMENT

Mercury 50, oleate of mercury 2, wool fat 30, white wax 5, white petrolatum 13. It contains from 49 to 51% of total mercury

### **Unguentum Hydrargyri Compositum** (*B.P.*)

Mercury ointment 10, yellow beeswax 6, olive oil 6, camphor flowers 3. Contains 12% of mercury. Is usually supplied for Scott's Dressing.

For enlarged glands, chronic synovitis and syphilitic nodes. Swelling of the ankles is well treated with it

**Unguentum Mercuriale** (*B.P.C.*) *Syn* UNGUENTUM HYDRARGYRI MITE, BLUE OINTMENT, TROOPER'S OINTMENT. A dilution of ointment of mercury 33½% with lard. Contains 10% Hg.

For destroying lice.

To promote the removal of the effusion of pleurisy, the rubbing into the chest of half a drachm of mercurial ointment twice daily is often useful.—Burney Yeo.

**Unguentum Hydrargyri Mite** (*U.S.P. XI*) *Syn* MILD MERCURIAL OINTMENT

Strong mercurial ointment 60, white wax 2, white petrolatum 38. It contains from 29 to 31% of total mercury.

### **Mercury Amalgam.**

This is one of the most popular of dental fillings. Black (Cosmos) suggests Silver 68.5, tin 25.5, zinc 1, gold 5.

In use, the alloy is worked up in a glass mortar with an equal quantity of mercury, and the excess of mercury is squeezed out immediately before filling in. It is the general rule to employ a double filling, i.e., to insert an initial filling of zinc oxysulphate or oxyphosphate, and afterwards an amalgam when a metal filling is employed, and where depth of the cavity will allow.

Amalgam fillings of teeth may cause mercury poisoning in susceptible people.—*Lancet*, 1/1926, 1275

[P1] **Hydrargyrum Ammoniatum** (*B.P., U.S.P. XI, P. Svec. X, P. Ned. V, P. Belg. IV*).  $\text{NH}_2\text{HgCl}$  - 252.1 *Syn* MERCURIC AMMONIUM CHLORIDE, WHITE PRECIPITATE.

A white powder obtained by the interaction of ammonia and mercuric chloride, insoluble in water but soluble in hydrochloric

acid. On prolonged contact with water a yellow basic salt is produced.

[P1] **Unguentum Hydrargyri Ammoniaci (B P)**

Strength 5% in simple ointment

In pruritus and other skin affections.

[P1] **Unguentum Hydrargyri Ammoniaci Dilutum (B P.C)**

Equal parts of the *B.P.* ointment and simple ointment.

Pustular eczema, resulting from pediculosis capitis in weakly children, is well treated with equal parts of this ointment and olive oil, enclosing the head in an oiled paper cap

[P1] **Unguentum Hydrargyri Ammoniaci et Zinci Oxidi (B P.C)** Equal parts of ointment of ammoniated mercury and ointment of zinc oxide

[P1] **Unguentum Hydrargyri Ammoniaci (U.S.P. XI)**

Ammoniated mercury 10, wool fat 5, white wax 5, white petrolatum 80.

*Tinea circinata* can be rapidly cured by this ointment

[P1] **Hydrargyri amido chloridum pulcherrimum (P. Dan)** is a 20% paste of freshly precipitated ammoniated mercury in wool fat and white soft paraffin for preparing ointments

[P1] **Unguentum Hydrargyri cum Paraffino (St. G. H.)** Ammoniated mercury 12 gr., oil of geranium 4 m., yellow soft paraffin to 1 oz. To be used sparingly with a camel hair brush, to the nose

[P2 81] **Hydrargyri Benzoas (Fr. Cx)**

$(C_6H_5COO)_2Hg, H_2O = 460.7$  *Syn.* MERCURIC BENZOATE

*Dose.*—*Per os*,  $\frac{1}{2}$  to  $\frac{1}{10}$  grain (0.0025 to 0.006 g.); by hypodermic injection—a daily dose of 1 to 2 ml., rising to 5 ml., of a 1% solution, made with the aid of 0.75% of sodium chloride in water; in preference with the addition of 0.75% to 1% of cocaine hydrochloride. Or weekly, 0.25 g. in 10% paraffin suspension

A white crystalline powder, practically insoluble in cold water but soluble with addition of salt, also soluble about 1 in 180 of alcohol 90%.

*Uses.* For treatment of syphilis

**Hydrargyri Bromidum.**  $HgBr_2 = 360.4$  *Syn.* MERCURIC BROMIDE

*Dose.*— $\frac{1}{16}$  to  $\frac{1}{4}$  grain (0.004 to 0.016 g.). Silvery scales

*Soluble* 1 in 250 of water, decomposes on boiling.

In syphilis, in solution with sodium bromide thus:—Mercuric bromide 1.8 g., sodium bromide 1.03 g., water 100 ml., is employed in dose of 1 to 2 ml. of the solution ( $\approx 0.01$  to 0.02 g. Hg) intramuscularly into the buttock. A platinum-iridium needle is essential. Some pain may be caused

[P1 81] **Hydrargyri Cyanidum (B.P.C., Fr. Cx, P.G. VI, P. Belg. IV).** *Syn.* MERCURY CYANIDE, CYANURETUM HYDRARGYRI  $Hg(CN)_2 = 252.6$

*Dose.*— $\frac{1}{16}$  to  $\frac{1}{4}$  grain (0.004 to 0.008 g.). *Fr. Cx* has max. single dose  $\frac{1}{4}$  grain, max. during 24 hours  $\frac{1}{4}$  grain approximately.

*Intravenous dose*—1 ml. of 1% solution considered a max. single dose, but more has been given, *see below*.



White or colourless, prismatic crystals. Soluble 1 in 13 of water, 1 in 3 of hot water, 1 in 4 of glycerin and 1 in 20 of alcohol 90%. It is not decomposed by alkalis.

**Uses.** It is used as a lotion to syphilitic sores, and given in pills of  $\frac{1}{10}$  gr. twice daily. Used in diphtheria,  $\frac{1}{10}$  gr. frequently, with 1 m. of tincture of aconite in honey, employing also a gargle, 1 in 10,000. Solutions of 1 in 1000 have been used in ophthalmia.

If given intravenously, as in combined organic arsenic and mercury treatment of syphilis, care must be taken to give strictly intravenously and not intramuscularly or hypodermically.

**SYPHILIS.** One injection of one of the neoarsphenamine preparations and five injections of 1% cyanide solution per week. Doses of the latter varied with tolerance of the patient, and it was found that many patients could stand 40 to 50 m. Superior to other routine methods.—J. Ernest Lane, *Lancet*, 11/1921, 796.

Syphilis, nasal and aural, treated by 1 ml. of 1% solution intravenously. Much used in France May occasion diarrhoea.—D Guthrie, *Practitioner*, Feb, 1920, 131

**ACUTE SYPHILITIC NEPHRITIS** Albuminuria disappeared after 15 days treatment with intravenous injections of 0.005 to 0.02 g., thus rendering possible the use of arsenic and bismuth, which were previously contraindicated.—Petges, *J Amer med Ass*, 1/1929, 1488

[P1 81] **Hydrargyri et Zinci Cyanidi (B.P.C.).** *Syn.* MERCURO-ZINC CYANIDE, LISTER'S SALT.

A white powder sometimes supplied tinted with rosalane (mauveine hydrochloride), obtained by precipitation from a cold saturated solution of the cyanide of mercury and potassium by adding a cold saturated solution of zinc sulphate in equimolecular proportions, or by adding in similar solutions mercuric chloride to zinc potassium cyanide. The maximum percentage of mercuric cyanide found is 38.5, and the body is usually regarded as an intimate mixture of the constituent cyanides.

**Solubility.** Very slightly in water, more so in dilute acids.

[P1 81] **Carbasus Hydrargyri et Zinci Cyanidi (B.P.C.)** *Syn.* DOUBLE CYANIDE GAUZE. Contains 0.5 to 1.5% of Hg, as  $Hg(CN)_2$ , and 1.5 to 3.0% of Zn, as  $Zn(CN)_2$ . It is a popular dressing for applying direct to wounds. It is not so irritant as some of the other mercurial dressings, and has the advantage of keeping well without the mercurial salt becoming reduced by the cotton. It may be damped before use with 1 in 20 phenol solution. Double cyanide wool and bandages contain about 3% of the double salt.

[P1 81] **Mercury and Zinc Cyanide Cream** may be made by triturating the powder with carbolic lotion 1 in 20 q.s., for applying to hairy parts adjacent to wounds.

[P1 81] **Mercury and Zinc Cyanide Paste.** Mercury and zinc cyanide 400, tragacanth 2, phenol 20, water 800, *mux.* For a first dressing for wounds. *Caution:* Not to be supplied in metal tubes—especially lead. The paste must be rubbed on, as thin a layer as possible.

[P1 81] **Mercury and Zinc Cyanide Lotion**, of strength 1 in 5000 to 1 in 1000, is used for wounds. *Caution:* Shake bottle—not dissolved.

**Hydrargyri Iodidum Flavum (B.P.C., U.S.P. XI, P. Helv V).**  $HgI_2$  — 327.5. *Syn.* YELLOW MERCUROUS IODIDE.

**Dose.**— $\frac{1}{2}$  to  $\frac{1}{4}$  grain (0.008 to 0.03). *U S P. XI* average dose  $\frac{1}{4}$  grain. *P. Helv. V* has max. single dose approx. 1 grain, max per day 3 grains.

Prepared by double decomposition between solutions of mercurous nitrate and potassium iodide. (Must not be confounded with the yellow variety of mercuric iodide).

Pills and tablets contain  $\frac{1}{4}$  grain Employed in syphilis

[P2 81] **Hydrargyri Iodidum Rubrum** (*B P, Fr Cx, P Helv V, P Dan.*)  $\text{HgI}_2 = 454.5$ . *Syn.* MERCURY BINIODIDE, MERCURIC IODIDE

**Dose** —  $\frac{1}{2}$  to  $\frac{1}{4}$  grain (0.002 to 0.004 g.). *Fr Cx* has max single dose  $\frac{1}{4}$  grain; max during 24 hours  $1\frac{1}{2}$  grains approximately

**Intravenously** —  $\frac{1}{2}$  grain (0.005 g.) in 75 minims (5 ml) is usual, but  $\frac{1}{4}$  grain (0.03 g) in 150 minims (10 ml) has been given — See R. L. Spittel's formula below.

Red powder, soluble in solutions of other iodides, and in solution of mercuric chloride, forming double salts, *cf.* mercuric potassium iodide, also 1 in 230 of olive oil, 1 in 25 of castor oil (100 parts of the latter will dissolve 8 of this iodide with 5 of mercuric chloride), about 1 in 150 of ether, 1 in 300 of alcohol 90%

**Uses.** A powerful antiseptic, less irritant than mercuric chloride As a lotion for the hands or eyes 1 in 5000 For wounds 1 in 7000, vaginal douche 1 in 10,000

More potassium iodide must be used to dissolve mercuric iodide than is indicated by the formation of the compound  $\text{HgI}_2 \cdot 2\text{KI}$ , otherwise  $\text{HgI}_2$  is precipitated on standing, at least an equal weight of potassium iodide should be used

*The strength of biniodide preparations should be expressed in terms of the active constituent,  $\text{HgI}_2$ . Statements of strength based on the theoretical content of double salts such as  $\text{HgI}_2 \cdot 2\text{KI}$ , or  $\text{HgI}_2 \cdot \text{KI} \cdot 1\frac{1}{2}\text{H}_2\text{O}$  are misleading A 1 in 1000 solution of  $\text{HgI}_2 \cdot 2\text{KI}$  is equivalent to less than 1 in 1700 of biniodide, and 1 in 1000 of  $\text{HgI}_2 \cdot \text{KI} \cdot 1\frac{1}{2}\text{H}_2\text{O}$  is equivalent to less than 1 in 1400*

If a douche is required in midwifery, 1 in 1000 biniodide always used. — A. P. Murtz, *Lancet*, ii/1926, 728

Biniodide should come into its own again in midwifery — *Brit med J.*, [1930, 359]

[P2] **Injectio Hydrargyri Iodidi Rubri** (Ragazzoni)

**Dose** — 2 to 6 minims (0.12 to 0.4 ml).

Mercuric iodide 1 gr., sodium iodide *q.s.*, in 64 m

In syphilis can be used in large doses, but is painful

[P2] **Injectio Hydrargyri Iodidi Intravenosa** (R. L. Spittel).

**Dose.**—120 to 180 minims (8 to 12 ml).

Mercuric iodide 3.24 g., sodium or potassium iodide 28.42 g., N/1 sodium hydroxide 40 drops or *q.s.*, water to 1000 ml. The solution is rendered carefully neutral, using phenolphthalein, the soda being added last. Often a single injection will produce an effect as phenomenal as arsphenamine Used in conjunction with latter in syphilis. — *Lancet*, i/1920, 378. **Caution** An average dose of this contains 0.03 g. ( $\frac{1}{4}$  grain) The amount of caustic soda in the formula in the *Lancet* paper was unnecessarily large the quantity needed is given above

**[P1-81] Injectio Hydrargyri Biniodidi (pro vagina)**

Mercuric chloride 8 gr., potassium iodide 24 gr., water to 1 oz. 1 drachm of this to a pint makes 1 in 10,000 approx.

**[P1] Lotio Hydrargyri Biniodidi (L.H.)**

Mercuric chloride 3 gr., potassium iodide 8½ gr., alcoholic solution of rosolic acid *q.s.*, distilled water to 10 oz. Strength of double salt 1 in 500

**[P1] Lotio Hydrargyri Biniodidi Spirituosus. Syn. BINIODIDE SPIRIT LOTION.**

Mercuric iodide 1, potassium iodide 1, alcohol 70% to 1000  
For gonorrhœa dilute solutions are used, also as a pigment or spray for throat in scarlatina and diphtheria

**[P1] Mistura Hydrargyri Biniodidi (K.C.H.).**

*Dose*—1 ounce (30 ml.)

Solution of mercuric chloride 30 m., potassium iodide 10 gr., ammonium carbonate 5 gr., decoction of cinchona to 1 oz.

**[P1] U.C.H.** has solution of mercuric chloride 60 m., potassium iodide 4 gr., water to 1 oz.

**[P1] Mist. Hydrarg. et Pot. Iod. (N.I.F.)**

Solution of mercuric chloride 1 dr., potassium iodide 5 gr., concentrated infusion of calumba 30 m., water to ½ oz.

The mercury in these mixtures is more rapidly eliminated than when given alone. The potassium iodide acts as a diuretic.

**[P2] Oleum Hydrargyri Biniodidi. Syn. HUILE D'IODURE MERCURIQUE (Fr. Cx.).**

*Dose*—15 minims (1 ml.), containing approx. ½ grain (0.004 gr.)

Mercuric iodide 4, olive oil, purified and sterilised, 920 by weight. Dissolve at not exceeding 60°

**[P1-81] Pilula Arsenii et Hydrargyri Iodidi.**

*Dose*—1 or 2, two or three times a day

Arsenous iodide, mercuric iodide, of each 1 gr., distilled water *q.s.* to dissolve, sugar *q.s.* to make 12 two-grain pills. May be combined with 2 gr. of iodide of iron

**[P2-81] Pilula Hydrargyri Iodidi Rubri (½ gr.) et Potassii Iodidi (4 gr.)**

*Dose*.—1 twice daily

**[P2-81] Solvellæ Hydrargyri Iodidi (B.P.C.)** contain 8½ gr. of mercuric iodide with sufficient potassium iodide, and eosin to tint, one dissolved in a pint of water gives a 1 in 1000 solution of mercuric iodide

**[P2-81] Unguentum Hydrargyri Iodidi Rubri (B.P.C.) 1 in 25**

For tinea may be applied to small spots, but not to large surfaces. Too strong for general use on the skin. Exophthalmic goitre has been treated by daily use of this ointment half strength

PARENCHYMATOUS GOITRE treated by dilute mercuric iodide ointment locally. Improvement in patient's general condition and comfort. —D. J. Harries, *Brit med. J.*, 1/1923, 555

**[P1] Unguentum Hydrargyri et Potassii Iodidi.**

Mercuric iodide 1, potassium iodide 1, water 13, lard 35, hydrous wool fat 50

**[P1] Wool, Mercuric Iodide. ½%.**

Impregnate absorbent wool 400 under pressure with a solution of mercuric iodide 1 and potassium iodide 1, and spread out to dry

**[P1-81] Hydrargyri et Potassii Iodidum.  $\text{HgI}_2, \text{KI}, 1\frac{1}{2}\text{H}_2\text{O}$  - 647.5**

A compound of this composition is obtained by crystallisation from the filtrate obtained on removing mercuric iodide formed by mixing solutions of mercuric chloride and potassium iodide. It is soluble 1 in 1 of alcohol 90%, 1 in 1 of ether and 1 in 2 of glacial acetic acid. It is not soluble in water except in presence of more potassium iodide

**[P2 81] Solubus Biniodide** (*Martindale, London*) contain mercuric iodide and potassium iodide equivalent to  $8\frac{1}{2}$  gr. of  $\text{HgI}_2, \text{KI}, 1\frac{1}{2}\text{H}_2\text{O}$ .

**Hydrargyri Iodidum Viride (B.P.C.).** *Syn.* GREEN MERCU-  
ROUS IODIDE, MERCURY PROTOIODIDE.

*Dose.*— $\frac{1}{4}$  to 1 grain (0.01 to 0.06 g.) gradually increased to 3 grains. Pills contain  $\frac{1}{4}$  and  $\frac{1}{2}$ ,  $\frac{1}{4}$  and  $\frac{1}{2}$  grain, and tablets contain  $\frac{1}{4}$  grain—with opium and pepper to prevent looseness of bowels.

**Incompatible** with other iodides.

A yellowish-green, odourless, tasteless powder containing mercurous iodide with free mercury. It should be kept from light, otherwise the mercurous iodide decomposes. Employed in syphilis.

**[P1 81] Hydrargyri Nitrates (P. Helv V)** *Syn.* MERCUROUS NITRATE  $\text{Hg}_2(\text{NO}_3)_2, 2\text{H}_2\text{O} = 561.3$

In colourless monoclinic crystals, generally damp (from adhering acid) and soluble in water, or yellow tinted (from basic salt), then not perfectly soluble in water. Used in syphilitic sores, 1 in 30 or more, as a lotion or ointment, and occasionally internally in same dose as mercuric chloride.

**[P1 81] Liquor Hydrargyri Nitratis Acidus (B.P.C.).**

Contains the equivalent of  $33\frac{1}{3}\%$  *w/w* of Hg dissolved in nitric acid.

*Fr. Cx.* dissolves mercury 100 in nitric acid (*Fr. Cx.*) 165 and water 35, mixed, with slight heat, and evaporates to 225 (all by weight). *Sp. gr.* 2.246

Used as a caustic for syphilitic warts, and lupus.

Diluted 1 in 1000, or more, is used as a urethral injection in gonorrhœa and as a gargle for syphilitic sore throat.

An intractable and extensive case of destructive facial lupus in a boy of 11 cured by painting the lesions on three occasions. Local reaction purulent and violent but no diarrhœa and no mercurial poisoning—W. J. O'Donovan, *Brit. J. Dermat.*, 1935, 353.

**[P1] Nebula Hydrargyri Nitratis (T.H.).** Strong ointment of mercuric nitrate 40 gr., yellow soft paraffin 40 gr., olive oil  $\frac{1}{2}$  oz., liquid paraffin to 1 oz.

**[P1] Pigmentum Hydrargyri Nitratis (B.P.C.).** *Syn.* GUTTÆ HYDRARGYRI NITRATIS.

Dilute mercuric nitrate ointment 1 in 16 in arachis oil.

*L.H.* has strong ointment of mercuric nitrate 60 gr., wool fat 30 gr., olive oil  $\frac{1}{2}$  oz., liquid paraffin to 1 oz.

**[P1] Pigmentum Hydrargyri Nitratis cum Menthole (B.P.C.)** resembles the preceding paint, but contains 1% *w/v* of menthol.

**[P1] "Nasal Oil" (St. M.H.)** is dilute mercuric nitrate ointment 20 gr., menthol 2 gr., lavender oil 5 m., olive oil to 1 oz.

**[P1] Unguentum Hydrargyri Nitratis Forte (B.P.).** *Syn.* CITRINE OINTMENT, MERCURIC NITRATE OINTMENT, UNG. HYDRARGYRI NITRATIS, STRONG OINTMENT OF MERCURIC NITRATE.

Contains about 1 of mercury in 15 of the finished ointment.

**[P1] Aurinarium Unguenti Hydrargyri Nitratis** contains  $\frac{1}{4}$  grain of ointment—useful for chronic eczema of the meatus.

**Unguentum Hydrargyri Nitratis Dilutum (B.P.)**

Contains 20% of strong ointment of mercuric nitrate with yellow soft paraffin.

In tinea tarsi of great value, employed with a brush to the eyelids, also in chronic eczema, psoriasis and herpes preputialis. In pustular eczema, after removing crusts, this checks further infection; Lassar's paste and soothing lotions may then be used.

**Unguentum Hydrargyri Nitratis Dilutum (R.L.O.H.).**

Strong ointment of mercuric nitrate 40 gr, yellow soft paraffin to 1 oz.

**[P1] Unguentum Hydrargyri Plumbi et Zinci (B.P.C.)**

*Syn.* UNGUENTUM METALLORUM.

Equal parts of strong ointment of mercuric nitrate, ointment of lead subacetate and ointment of zinc oxide.

*K.C.H.* is same as *B.P.C.* except for lead acetate ointment instead of lead subacetate ointment. *M.H.* is same as *B.P.C.* except for dilute mercuric nitrate ointment instead of strong. *W.H.* has equal parts of dilute mercuric nitrate ointment, lead acetate ointment and ointment of zinc oxide. *L.S.H.* has mercurous chloride 10 gr, zinc oxide 20 gr, lead acetate 10 gr., strong ointment of mercuric nitrate 10 gr, benzoinated lard to 480 gr. *St J.H.* has mercurous chloride 10 gr, zinc oxide 20 gr, lead acetate 10 gr, dilute mercuric nitrate ointment to 480 gr.

**Unguentum Hydrargyri cum Plumbo (St M H.)** contains lead acetate 10 gr, mercurous chloride 10 gr, zinc oxide 24 gr, strong mercuric nitrate ointment 24 gr, olive oil *q.s.*, lard to 480 gr

**[P2 81] Phenylmercuric Nitrate.** *Prop Name* MERFENIL (*Pharmaceutical Specialties (May & Baker) Ltd, London*).

An almost white basic salt,  $C_6H_5HgOH, C_6H_5HgNO_3$ , sparingly soluble in water, more soluble in diethylene glycol.

It may be obtained by adding a solution of nitrogen tetroxide in ice-cold chloroform to an ice-cold solution of diphenylmercury in chloroform. After standing overnight at  $0^\circ$  the product is filtered. The precipitate is recrystallised from moist alcohol

**Uses.** As a germicide with low toxicity and only slightly less active in presence of body fluids 1 in 3000 for skin disinfection, 1 in 1500 for wounds, fistulæ, etc., 1 in 1000 for mycotic infections, and 1 in 30,000 as vaginal douche

Clinical studies indicate that this preparation is of great utility in the treatment of a wide variety of infections due to bacteria and fungi. Infections with the protozoon *T. vaginalis* also yield to basic phenylmercuric nitrate. It is used in the form of an aqueous 1 in 1500 solution. That given to the patient for dilution in the preparation of a douche is a 1% solution in diethylene glycol, a drachm to a quart of warm water making approximately a 1 in 25,000 solution.—L. H. Biskind, *Lancet*, ii/1935, 1049.

**TINEA AND EPIDERMOPHYTOSIS.** Affected parts thoroughly cleansed with soap and water and a soft brush, and a 1 in 1500 ointment in a hydrophilic base containing cholesterol derivatives, gently rubbed in night and morning (over-treatment must be avoided). 205 out of 285 cases cured.—B Levine, *J. Amer med Ass*, ii/1933, 2108

[P1] **Hydrargyri Oxidum Flavum** (*B.P., P. Helv. V*)

An orange-yellow amorphous powder obtained by interaction of mercuric chloride and sodium hydroxide.

**Insoluble** in water or alcohol 90%.

**Uses.** In ointments for inflamed eyelids. Should not be used whilst patient is taking iodide—violent irritation may be produced. Syphilitic sores and eczema may be treated by the 1% ointment.

The favourable results reported with ointments of yellow mercuric oxide in blepharitis are probably due to the vehicle softening the crusts, which allows their removal without disturbing the tissue of the lid margins, and to prevention of maceration of the tissue by excess of tears. Petrolatum alone or with hydrous wool fat is more agreeable to the patient and just as effective. It is difficult to see how a relatively insoluble drug, each particle of which is thickly coated with an insoluble vehicle, can diffuse into the skin, conjunctiva or tears in sufficient quantity to be of any value as an antiseptic. Pagenstecher only recommended its use in phlyctenular conjunctivitis and keratitis, and for this condition it is still valuable at a certain stage—G. N. Hosford and J. P. McKenney, *J. Amer. med. Ass.*, 1/1933, 19.

[P1] **Lotio Hydrargyri Flava** (*B.P.C.*). *Syn.* YELLOW WASH.

Contains mercuric oxide precipitated from 0.5% *w/v* of mercuric chloride by solution of calcium hydroxide.

[P1] **Oculentum Flavum** (*B.P.C.*) contains 10% of moist yellow mercuric oxide ointment equivalent to 1% of yellow mercuric oxide.

[P1] **Oculentum Hydrargyri Oxidi** (*B.P.*) contains 1% of yellow mercuric oxide.

[P1] **Pagenstecher's Ointment** was originally prepared with a basis of spermaceti ointment. In this country yellow mercuric oxide 4% in yellow soft paraffin is usually supplied.

[P1] **Pasta Flava** (*Gt. Orn. H.*). Yellow mercuric oxide 15 gr., zinc paste to 1 oz. (Zinc paste contains starch 108 gr., zinc oxide 108 gr., simple ointment to 1 oz.).

[P1] **Unguentum Hydrargyri Oxidi Flavi** (*B.P.C.*) 2% in yellow soft paraffin.

[P1] **Unguentum Hydrargyri Oxidi Flavi** (*U.S.P. XI*)

Yellow mercuric oxide 1, liquid petrolatum 1, wool fat 5, yellow wax 5, petrolatum 88

[P1] **Unguentum Hydrargyri Oxidi Flavi** (*R.L.O.H.*) contains 2, 4 or 8 gr of freshly precipitated mercuric oxide, pressed as free from moisture as possible, in yellow soft paraffin to 1 oz. The precipitation may be carried out as described in the *B.P.C.* for *Ung. Hydrarg. Ox. Flav. Humid.*

[P1] **Unguentum Hydrargyri Oxidi Flavi Humidi** (*B.P.C.*) contains 10% of freshly precipitated and very finely divided yellow mercuric oxide in a wool fat and soft paraffin basis. To be diluted for ophthalmic use as required.

[P1] **Hydrentum** (*Allen & Hanburys, London*) Neutral ointment of yellow mercuric oxide in strengths of 0.25 to 5%; also with [P1 81] atropine 0.5 and 1%. For ophthalmic use.

[P1] **Hydrargyri Oxidum Rubrum** (*B.P.C., P. Helv. V, P. Dan.*). *Syn.* RED PRECIPITATE.  $\text{HgO} = 216.6$ .

**Dose.**— $\frac{1}{4}$  to  $\frac{1}{2}$  grain (0.004 to 0.016 g.).

A red crystalline powder obtained by heating mercurous nitrate; chemically it is identical with the yellow oxide

[P1] **Unguentum Hydrargyri Oxidi Rubri** (B P C) *Syn.* RED PRECIPITATE OINTMENT. 1 in 10.

For use in chronic skin affections

[P1] **Pommade de Lyon.** Red mercuric oxide 1, yellow soft paraffin 15

[P1] **Hydrargyri Oxycyanidum** (B.P., *P. Helv V*, *P. Dan*)  $\text{HgO}, 3\text{Hg}(\text{CN})_2 = 974.5$ .

*Dose*—By intramuscular injection,  $\frac{1}{2}$  to  $\frac{1}{4}$  grain (0.005 to 0.01 g.); by intravenous injection,  $\frac{1}{8}$  grain (0.01 g.)  $\frac{1}{16}$  to  $\frac{1}{8}$  grain (0.004 to 0.01 g.) may be given orally

**CHEMICAL COMPOSITION** Contains about 21% of HgO and 78% of  $\text{Hg}(\text{CN})_2$ . *P. G. VI* requires 33.3 to 35.2% of  $\text{Hg}(\text{CN})_2, \text{HgO}$ , equivalent to 15.37 to 16.25% of HgO and 84.6 to 83.8% of total mercury cyanide. It is a mixture of approx 34% mercury oxycyanide and 66% mercury cyanide

*P. Svec. X* is a mixture of the oxycyanide,  $\text{Hg}(\text{CN})_2, \text{HgO}$ , and cyanide, containing 30 to 40% of oxycyanide

*P. Helv V* gives  $\text{HgO}, \text{Hg}(\text{CN})_2$ , but the characters and tests agree rather with the compound  $\text{HgO}, 3\text{Hg}(\text{CN})_2$ . *P. Belg IV* contains the two compounds. The true oxycyanide is liable to explode when heated.

**Soluble** 1 in about 18 of water. The solubility varies with the proportion of HgO present

**Uses.** In the treatment of syphilis during first week 0.05 g in pill *per diem* as an average has been given—to be taken when the stomach is full. Should not be used with potassium iodide.

As a wound lotion 0.2 to 0.6% solutions have been employed, 1 in 5000 to 1 in 10,000 as bladder irrigant, in eye work 1 in 1000 to 1 in 5000, and 1 in 200 for instruments, which it is said not to attack.

Gonorrhœa treated by irrigation with mercury oxycyanide 1 in 2000, also potassium permanganate 1 in 6000 for acute, to 1 in 2000 for chronic cases—H. J. Blakesley, *Brit med J*, 1/1921, 619

Mercury oxycyanide is good against staphylococci but is an indifferent gonocide—H. D. L. Spence, *Lancet*, 1/1930, 19

[P1] **Lotio Hydrargyri Oxycyanidi** (R L O H.).

$\frac{1}{2}, \frac{1}{8}$  or  $\frac{1}{10}$  gr. in water 1 oz

Hypopyon ulcers treated by subconjunctival injections—T. L. de Courcy, *Brit. med. J*, 11/1921, 737. Cf. *Injectio Hydrargyri Cyanidi*

[P1] **Lotio Hydrargyri Oxycyanidi cum Zinci Sulphate** (R L O H.)

Mercuric oxycyanide  $\frac{1}{2}$  gr, zinc sulphate  $\frac{1}{2}$  gr, water to 1 oz

[P1] **Mercury Oxycyanide Lotion Sterules** (*Martindale, London*) contain 8.75 grains. Each diluted to 1 pint makes 1 in 1000 solution, to 1 quart makes 1 in 2000 solution, 1 in 5 pints makes 1 in 5000 solution.

[P1] **Pasta Hydrargyri Oxycyanidi** (L H.)

Mercuric oxycyanide 24 gr, tragacanth 192 gr, glycerin 4 oz, distilled water to 20 oz. Sterilise

[P1] **Solvellæ Hydrargyri Oxycyanidi** (B.P.C.) contain 4.375 gr of mercuric oxycyanide coloured with eosin. One dissolved in 1 pint of water gives a 1 in 2000 solution

[P2 81] **Hydrargyri Peptonas.** *Syn.* MERCURY PEPTONATE

*Dose per os.*— $\frac{1}{4}$  grain (0.03 g) increased with caution; hypodermically  $\frac{1}{4}$  grain

A brown powder containing 10% of mercuric chloride, soluble in water

*Fr. Cx.* gives method of manufacture of a solution

[P2 81] **Mercuriol Tablets** (*Parke, Davis, London*) contain 1 gr. of nucleinate of mercury *Dose*—1 to 2 tablets For the treatment of syphilis

[P2 81] **Hydrargyri Perchloridum** (*B.P.*).  $\text{HgCl}_2 = 271.5$

*Syn.* HYDRARGYRUM BICHLORATUM (*P. Helv. V.*), HYDRARGYRI BICHLORIDUM (*U.S.P. XI.*), MERCURIC CHLORIDE, HYDRARGYRI CHLORIDUM CORROSIVUM, CORROSIVE SUBLIMATE

*Dose*— $\frac{1}{32}$  to  $\frac{1}{16}$  grain (0.002 to 0.004 g), but it may be increased to  $\frac{1}{4}$  grain. *Fr. Cx.* has max single dose  $\frac{1}{4}$  grain; max during 24 hours 1 grain approximately. Intravenously  $\frac{1}{32}$  grain increased, v p 548

In heavy colourless crystalline lumps or white powder.

**Antidotes and Treatment of Mercurial Poisoning.** In addition to the references below, see p 535

It is rare for patients to die who have not swallowed more than 7  $\frac{1}{2}$  grains. Gastric lavage only helpful in first 15 minutes, repeated venesections and transfusions worth while, also biliary drainage and colonic irrigation—E R Mintz, per *Brit med. J. Epit.*, 11/1933, 64

Some measure of success (only 3 deaths in 48 cases) in corrosive sublimate poisoning from a therapeutic scheme comprising gastric lavage and colonic irrigation by a 5% solution of sodium bicarbonate and an internal administration of the salt in a dosage sufficient to maintain the urine alkaline to litmus—W B Porter and C E Simons, *Amer. J. med. Sci.*, Sept., 1934, 375

**Soluble** 1 in 18 of water, 1 in 4 of alcohol 90%, 1 in about 4 of ether, 1 in 2 of glycerin. More soluble double salts are formed in solution with sodium, ammonium and other chlorides. These solutions contain fewer mercuric ions and are hence less poisonous (taking same weights of mercury) than  $\text{HgCl}_2$ . They are not more antiseptic.

**Incompatibles.** It precipitates most alkaloids from solutions and should therefore not be ordered with them. Interaction also occurs with alkalis and their salts and with the salts of silver and lead. Steel surgical instruments should not be dipped in this solution. It forms insoluble compounds with albuminous fluids, and is also incompatible with bodies containing tannin, soap, iodine and potassium iodide.

**Uses.** As antiseptic, but is precipitated by proteins. For the skin and for general use, a 1 in 1000 solution is used. The antiseptic action is more marked if alcohol 70% is used as the solvent. For irrigation of wounds and for fistulæ 1 in 10,000, and for vaginal douches 1 in 100,000, but stronger solutions are frequently used. In eye lotions and in mouth-washes for glossitis and syphilitic ulceration 1 in 5000 to 10,000 may be used. Urethral injections in gonorrhœa may contain 1 in 4000. The 1 in 1000 solution with hydrochloric acid 2 in 1000 is often effective in prickly heat. Internally the perchloride is given in syphilis. Small doses, e.g.,  $\frac{1}{16}$  to  $\frac{1}{8}$  grain, have been given intravenously in septicæmia

A fatal case following the self-application to the vagina of a solution of a 7-grain tablet in a pint of warm water.—B. Russell, *Brit med. J.*, i/1934, 756.



**EMPHYEMA, PNEUMOCOCCAL.** Irrigation of the pleural cavity with 1 in 40,000 mercuric chloride, in treatment. (1 in 20,000 kills the pneumococcus in 2 hours—Choyce's *Surgery*).—F. J. Hathaway, *Brit. med. J.*, i/1925, 632.

**CATARACT OPERATION.** By washing the eyes with mercuric chloride 1 in 6000 before and after cocaine anæsthesia, sepsis is abolished—E. R. Shetti, *Brit. med. J.*, ii/1930, 1098

**GUINEA WORM.** Emily, a French naval surgeon, succeeded in killing the parasite by injecting mercuric chloride solution 1 in 1000 into the body of the worm—Sir P. Manson, *Tropical Diseases*. See also J. Graham Forbes, *Lancet*, i/1920, 837. Injections tried subcutaneously into the protruding head

**OPHTHALMIA NEONATORUM.** Dangerous in treatment of (especially in conjunction with silver nitrate drops)—4 recent cases quoted. Frequent washing out with normal saline or saturated boric acid solution safe and effective—D. Forbes, *Lancet*, ii/1931, 1102.

**SUPPURATIVE OTITIS MEDIA.** Mercuric chloride in glycerin 1 in 1000 successful where all other treatments have failed. Phenol in glycerin equally good.—T. P. Lowe, *Lancet*, ii/1928, 256

#### **Intravenous Injection of Perchloride.**

**ACUTE BACTERIAL INFECTIONS**, e.g., pneumonia, well treated by intravenous injections of  $\frac{3}{4}$  or  $\frac{1}{4}$  grain—J. Burnford, *Lancet*, i/1926, 312.

Bacterial infection, 330 cases, treated with mercuric chloride or mercuriochrome, or both. 5 ml. of 1 in 1250 solution of mercuric chloride ( $\frac{1}{4}$  grain) in saline as a first dose, repeated if necessary in 12 to 24 hours, according to patient's condition. Maximum dose 7 ml. Solution freshly prepared and injected directly into a vein. Among the complications cited are thrombosis, diarrhoea, stomatitis and nephritis—L. S. Dudgeon, *Lancet*, i/1926, 169.

**DIURETIC ACTION** of mercuric chloride dissolved in serum injected intravenously is marked.—K. I. Melville and R. L. Stehle, *J. Pharmacol.*, Oct, 1928, 222.

**PNEUMONIA**, lobar and lobular, acute staphylococcic infections, chorea and subacute rheumatism, chronic infective arthritis of undetermined origin and encephalitis lethargica. Mercuric chloride intravenously in doses of  $\frac{1}{4}$  grain to  $\frac{1}{2}$  grain is very useful, e.g.,  $\frac{1}{4}$  grain in normal saline 8 ml. Intestinal irritation may occur—H. Pritchard, *Brit. med. J.*, i/1927, 794.

[P2] **Carbasus Hydrargyri Perchloridi (B.P.C.).** *Syn.* **SUBLIMATE GAUZE.** Contains about 0.1% of mercuric chloride when fresh, but the strength is very variable.

[P2] **Lint, Absorbent Wool or Wood Wool**, may also be impregnated with  $\frac{1}{2}$ % each of corrosive sublimate and glycerin

[P2] *P. Jap. IV* uses mercuric chloride 2, potassium chloride 2, water 1500, wool 1000, i.e., 0.2%. Faintly coloured with scarlet or fuchsin "S"

[P2] **Collyrium Hydrargyri Perchloridi (B.P.C.).** 0.02% w/v.

[P2] **Collyrium Hydrargyri Perchloridi (N.I.F.)**

Mercuric chloride solution 1, distilled water to 3. For use dilute with equal quantity of water: strength when diluted 1 in 6000

[P1] **Mackenzie's Eye Wash.**

Mercuric chloride 1, ammonium chloride 6, extract of belladonna 10, cochineal  $\frac{1}{4}$ , proof spirit 55; rub together and add water to 330. Mix with equal parts of boiling water to bathe the eyes. *Caution.*—This is about five times as strong as usually employed.

[P2] **Collyr. Acid. Boric c. Hydrarg.** (N.I.F.). Solution of mercuric chloride  $\frac{1}{4}$  oz., boric acid 90 gr., distilled water to 6 oz

[P2] **Gargarisma Hydrargyri Perchloridi** (1 in 1750). Mercuric chloride  $\frac{1}{4}$  gr., hydrochloric acid 1 m., glycerin 30 m., water to 1 oz.

For influenza, sore throat, especially quinsy, solution of mercuric chloride 1, acid infusion of rose petals 1. 1 tablespoonful in a teacupful of hot water as a gargle.

[P2] **Gargarisma Hydrargyri Perchloridi (T.H.).** Mercuric chloride  $\frac{1}{4}$  gr., glycerin 24 m., water to 1 oz.

**[P2 81] Glycerinum Hydrargyri Perchloridi (R.L.O.H.)**

Mercuric chloride 4, 8 or 16 gr., glycerin to 1 oz. [P2] *U C.H.* has 0.1% *L.H.* uses mercuric chloride 17½ gr., water 6 dr., glycerin to 2 pints, tinted blue To be distinguished from the following —

**[P2 81] Glycerinum Hydrargyri Perchloridi Alcoholicum (U C.H.)** *Syn* GLYCERIN-ALCOHOL-PERCHLORIDE. Mercuric chloride 35, glycerin 50, methyl blue 0.05, methylated spirit to 100. For disinfecting urine 1 dr. to a pint

**[P2] Injectio Hydrargyri Perchloridi (Intravenous) (Gt Orm H)** contains ⅒ gr (0.0015 g.) in normal saline 85 m (5 ml.) for children under 2 years For older children ⅒ gr (0.002 g) in the same volume. May be repeated on three successive days

**[P2] Liquor Hydrargyri Perchloridi (B.P.).** *Syn.* VAN SWIETEN'S SOLUTION (*Fr. Cx*). 1 in 1000, ⅒ gr. in 1 drachm approx.

*Dose.*—½ to 1 drachm.

**[P2] Liquor Hydrargyri Perchloridi Acidus (C.X.H.)** *Syn* HARRINGTON'S SOLUTION

Solution of mercuric chloride 8, hydrochloric acid 6, industrial methylated spirit 64, solution of methylene blue (2%) 0.2, distilled water to 100. For pre-operative preparation of the skin

**[P2] Liquor Hydrargyri Perchloridi Acidus (St T H)** *Syn* TYPHOID SOLUTION Mercuric chloride 1 oz., hydrochloric acid (strong) 25 oz., water to 500 oz Used only as disinfectant for excreta

**[P2] Lotio Hydrargyri Acetica.**

Mercuric chloride 1, acetic acid 75, glycerin 75, alcohol (90%) 250, rose water 500. To destroy pediculi and detach their ova

**[P2] Lotio Hydrargyri cum Acido Carbolico (P E H C)**

Solution of mercuric chloride 20 m, dilute acetic acid 40 m, oil of turpentine 2 dr., solution of phenol (1 in 40) to 1 oz. For pediculi

**[P2] Lotio Hydrargyri cum Oleo Terebinthinae (U C H)**

Mercuric chloride 0.6, industrial methylated spirit 12.50, oil of turpentine to 100.

**[P2] Lotio Hydrargyri Perchloridi (U C H)** Mercuric chloride 0.2% coloured with turquoise blue *St T H.* is the same, coloured with methylene blue *L.H.* and *C H W* are 1 in 1000 *R L O.H.* ⅒, ⅓, ⅓, or ⅓ grain in 1 ounce The three last not coloured *W H* has ⅒ gr in 1 oz with 15 m of glycerin

**[P2] Lotio Parasitica (St. M. H.).**

Mercuric chloride ⅒ gr, acetic acid 2 dr., water to 1 oz

**[P2] Mistura Hydrargyri Perchloridi (Gt Orm H)** (*Dose* for 1-year-old child)

Solution of mercuric chloride 5 m, glycerin 5 m, water to 1 dr. For infective diarrhoea of infants, in conjunction with small (5 m) doses of castor oil

**[P2 81] Pigmentum contra Tineam.**

Mercuric chloride 1, salicylic acid 9, phenol 10, glycerin 80 Efficient in ringworm

**[P2 81] Pigmentum Hydrargyri Perchloridi (T.H.)**

Mercuric chloride 1, glycerin 25, water 75 A potent solution to be used with very great caution and by the surgeon only Not more than one application to be made

**[D P1 81] Pilules de Chlorure Mercurique Opiacées (Fr Cx)** DUPUYTRIN'S PILLS.

Mercuric chloride 1, extract of opium 2, extract of agropyrum 2, powdered liquorice q.s. For 100 pills Each pill contains mercuric chloride 0.01 g and extract of opium 0.02 g

**[P2-81] Solvellæ Hydrargyri Perchloridi (B.P.C)** contain 8½ gr of mercuric chloride with sodium chloride, and methylene blue to colour. One dissolved in 1 pint of water gives a 1 in 1000 solution

**[P2 81] Toxibellæ Hydrargyri Bichloridi Magnæ (U.S.P XI)** *Syn* LARGE POISON TABLETS OF MERCURY BICHLORIDE, LARGE CORROSIVE SUBLIMATE TABLETS

They contain about 0.5 g. of HgCl<sub>2</sub> in each tablet, and must be of a distinctive colour and not discoid in shape; the *U S P XI* requires that when sold for

household use they must be packed in glass bottles of distinctive angular shape with irregular or roughened sides or edges, with a red label marked "POISON" and the weight of  $\text{HgCl}_2$  in each tablet stated thereon.

[P2 81] **Toxittabellæ Hydrargyri Bichloridi Parvæ** (U S P XI) SMALL POISON TABLETS OF MERCURY BICHLORIDE.

They contain about 0.125 g. of  $\text{HgCl}_2$ , and must be prepared and packed as described above (see *Toxittabellæ Hydrargyri Bichloridi Magnæ*, U S P).

[P2] **Unguentum Desinficiens** (NEISSER-SIEBERT) (*P Svec. X*) Triturate tragacanth 20 g and wheat starch 40 g with glycerin 170 g. Dissolve separately gelatin 7 g. in warm water 500 ml and add mercuric chloride 3 g and sodium chloride 10 g to this solution. While still warm add with stirring the tragacanth mixture. Warm on water bath until homogeneous. When cool add alcohol 90% 250 g. in small lots.—Swedish Medical Board, *Chem. & Drugg*, ii/1922, 204.

[P2] **Unguentum Hydrargyri Perchloridi Compositum** (L.H.)

Mercuric chloride 2 gr., phenol 20 gr., glycerin 10 m., olive oil 40 m., zinc ointment to 1 oz

[P2 81] **Sublamin** (*Schering, London*). MERCURY SULPHATE ETHYLENEDIAMINE. A non-irritating substitute for sublimate, superior in penetration because of absence of albumin precipitation. Supplied in 15-gram tablets

[P1] **Sal Alembroth**. *Syn* AMMONIO-MERCURIC CHLORIDE

$(\text{NH}_4)_2\text{HgCl}_4 \cdot \text{H}_2\text{O} = 396.5$

A crystalline powder. Is a powerful antiseptic, but does not combine with albumin quickly and hence is not very irritating.

**Uses.** Formerly used for [P1] medicating dressings, bandages, gauze, wool gauze, and wool tissue, 1 or 2% (which are dyed blue), also as an intramuscular injection for syphilis. (*Dose.*—10 minims of 5% solution. Painful. Slowly eliminated.)

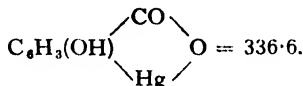
**Soluble** 2 in 1 of water, 1 in 4 of alcohol 90%, also in glycerin

[P2 81] **Hydrargyri Salicylas** (B.P.C., U.S.P. XI, *P Helv V*).

*Dose.*— $\frac{1}{20}$  to  $\frac{1}{4}$  grain (0.003 to 0.02 g.) Intramuscularly,  $\frac{1}{10}$  grain in 10 minims of liquid paraffin, increased up to 1 grain (Cocaine salicylate may well be added). U.S.P. XI average dose, intramuscularly, 1 grain twice a week. P.G. VI gives maximum single dose  $2\frac{1}{2}$  grains (0.15 g.). It is also official in *P Ital V*

A white powder containing 54 to 59.6% of Hg.

When produced by the interaction of mercury oxide and salicylic acid, the chief constituent is anhydro-hydroxy-mercuric-salicylic acid of formula



Almost insoluble in water (but soluble in solutions of sodium hydroxide and sodium carbonate), scarcely soluble in alcohol 90%. This is the basic mercuric salicylate as distinguished from the neutral or normal salt (see below)

**Used** as an antiseptic and antisyphilitic and as a dusting powder or ointment for sores. Should not be given in large doses with potassium iodide.

As an injection for gonorrhœa 15 minims of a mucilage suspension 1–300 has been used.

**BELL'S PALSY.** Three to four injections intramuscularly in 10 to 14 days of 10 m. of 1% suspension of mercury salicylate in liquid paraffin gave excellent results.—P. A. Harry, *Prescriber*, 1926, 290.

**LOCAL SKIN AFFECTIONS** well treated with mercury salicylate in liquid paraffin injections intramuscularly, 1 gr. per ml dose —W A Elliott, *Brit. med J.*, 1/1925, 551

The injection of mercury salicylate intramuscularly artificially induces leucocytosis. This accounts for its beneficial action in certain cases of syphilis, in furunculosis, and small infected wounds, and in trachoma. One to three injections often give good results in asthma, hay fever, arthritis, bronchiectasis, and skin complaints. Encephalitis lethargica well treated by 4 injections, each of 1 gr of mercury salicylate in oily suspension —Burr Ferguson, *Lancet*, 1/1925, 1292.

In rabbits, mercury salicylate appears to be more rapidly absorbed when in oily suspension, in which instance its lethal dose is 0.03 g per kilo —*J. Pharmacol.*, June, 1926, 388

[P2 81] **Hydrargyri Salicylas, Neutrale.**  $(C_6H_4 \cdot OH \cdot COO)_2Hg$  = 474.7 *Dose.*—Hypodermically  $\frac{1}{16}$  to 1 grain suspended 1 in 10 in liquid paraffin. Comparatively non-irritant

Quinine-urea (2%) added as follows relieves pain —

Quinine-urea 2, water 2, dissolve and mix with wool fat 20. To this add mercuric salicylate 10, liquid paraffin *q s.* to 100

[P2 81] **Merthiolate** (*Lilly, London*) SODIUM ETHYLMERCURITHIOSALICYLATE,  $C_2H_5 Hg S \cdot C_6H_4 COONa$

Contains 49% of Hg in organic combination. A potent germicide for sterilising tissue surfaces. Less toxic than mercuric chloride. For general application 1 in 1000 isotonic solution, for mucous membranes 1 in 2000 to 1 in 5000

**Hydrargyri Subchloridum (B.P.)** *Syn and Prop. Name* MERCUROUS CHLORIDE, CALOMEL (*P. Dan.*), SUBCHLORIDE OF MERCURY, MERCURIUS DULCIS (*P. Ned. V.*), HYDRARGYRI CHLORIDUM MITE (*U.S.P. XI.*), HYDRARGYRUM CHLORATUM (*P. Helv. V.*), PRÉCIPITÉ BLANC (*Fr. Cx.*, *F.E. VIII.*) (distinguish from British and *P. Belg. IV* white precipitate which is Hydrargyrum Ammoniatum), LEMOIAC (a light variety) (*Howards, Ilford*).  $HgCl = 236.1$ .

*Dose.*— $\frac{1}{2}$  to 3 grains (0.03 to 0.2 g.), by intramuscular injection  $\frac{1}{2}$  to 1 grain (0.03 to 0.06 g.). *U.S.P. XI* average laxative dose  $2\frac{1}{2}$  grains. *Fr. Cx.* has maximum single dose 15 grains, maximum during 24 hours, 15 grains. *P. Helv. V* has approx. 3 grains and 10 grains respectively

Heavy white powder. It can also be obtained as small, soft, scaly crystals for eye work (*see Duret's calomel, Vol. II.*)

**Insoluble** in water, ether or alcohol

**Incompatible** with acids, alkalis (*see Lotio Nigra*), with sodium and potassium chloride and with bromides, iodides, sulphur, cherry laurel water, and antipyrin. With regard to calomel and sodium chloride, the usual view is that mercuric chloride may be formed.

**Uses.** Alterative, purgative and anti-syphilitic. Was always considered a cholagogue, but at the present time is thought to empty the gall-bladder only, not to increase the actual amount of bile formed. Most useful purgative for congested liver and dyspepsia generally. To be given at bed-time followed by morning saline draught. Useful where there is intestinal putrefaction, *e.g.*, in dysentery, faecal accumulation, typhoid. For torpid liver  $\frac{1}{4}$ -grain

doses hourly valuable and repeated small doses, *e.g.*,  $\frac{1}{2}$  gr every hour for 12 to 18 hours, may abort a quinsy if used before suppuration occurs. As dusting powder to ulcers and many skin diseases (but not to the cornea of the eye if potassium iodide is being given) Applied dry relieves pruritus ani. Administered by intramuscular injection in syphilis, calomel is painful but highly active

**AMEBIC DYSENTERY** Calomel in doses of 0.03 g 12 times a day for 3 days, followed by 3 days' treatment with bismuth subnitrate 0.5 g 12 times daily — G Beijnen, per *J. trop. Med. (Hyg.)*, 1923, 256.

**ASIATIC CHOLERA** might well be treated with 5 gr hourly doses of calomel — increasing to 10 gr. if necessary. — W. E. Fellowes, *Brit. med. J.*, ii/1921, 176

**GALL STONES** are often expelled after large doses of calomel followed by castor oil. — Whittle, *Pract. Med.*

**Injectio Hydrargyri Subchloridi (B.P.).** *Syn.* CALOMEL INJECTION.

**Dose.**—By intramuscular injection, 10 to 20 minims (0.6 to 1.2 ml).

Contains about 5% *w/v* of very finely powdered mercurous chloride with camphor and creosote in wool fat and olive oil.

[P2] **Injectio Hydrargyri Subchloridi Hypodermica.** Lambkin's original formula.

**Dose.**—10 minims injected once a week.

Calomel 10 gr, suspended in  $\frac{1}{2}$  oz. of sterile olive oil containing 2% of phenol.

Morphine  $\frac{1}{4}$  gr. may be given afterwards to relieve pain.

Poisoning, fatal, from intramuscular calomel injections. — *Brit. med. J. Epit.*, i/1922, 49.

[P1] **Gargarisma Hydrargyri et Potassii Chloratis (T.H.)**

Black wash 2 dr., gargle of potassium chlorate  $\frac{1}{2}$  oz. (gargle of potassium chlorate contains potassium chlorate 12 gr., sodium bicarbonate 6 gr., potassium bicarbonate 6 gr., water to 1 oz.)

[P1] **Lotio Hydrargyri Nigra (B.P.).** *Syn.* BLACK MERCURIAL WASH, BLACK WASH.

Contains mercurous oxide equivalent to 0.7% of mercurous chloride with glycerin and solution of calcium hydroxide.

[P1-S1] **Pilulæ Hydrargyri Subchloridi Compositæ (B.P.C.).** *syn.* PLUMMER'S PILLS, **dose**—1 or 2 pills, contain mercurous chloride 1 gr., sulphurated antimony 1 gr., guaiacum resin 2 gr.

**Pilula Hydrargyri Subchloridi, Rhei, Cascaræ et Capsicini.**

Calomel  $\frac{1}{2}$  gr., extract of rhubarb 2 gr., extract of cascara 1 gr., capsicin  $\frac{1}{2}$  gr. Relieves constipation, *e.g.*, that arising from large doses of bismuth

[P1-S1] **Pulvis Basilicus.**

**Dose.**—For a child of 2 years, 4 grains (0.25 g.), of 6 years or upwards, 8 grains (0.5 g.).

Mercurous chloride 3, scammony 3, potassium acid tartrate 3, jalap 1, ginger 1, antimonial powder 1.

**Pulvis Hydrargyri Subchloridi Compositus (St. J. H.)**

Mercurous chloride 1 dr., zinc oxide 1 dr., starch 3 dr., talc 3 dr

**Unguentum Hydrargyri Subchloridi (B.P.).** *Syn.* CALOMEL OINTMENT. Mercurous chloride 1, simple ointment 4. To relieve irritation.

**Calomel Cream (L.L.).** Calomel 10 gr. to soft paraffin 1 oz. Distinguish from that of Lambkin—*q.v. supra.*

**1) Unguentum Hydrargyri Subchloridi Compositum**(I.P.C.). *Syn.* CALOMEL CREAM, PROPHYLACTIC OINTMENT

Mercurous chloride 25%, and mercuric oxycyanide 0.075%, in a wool fat and paraffin basis.

For prophylactic measures against syphilis, Metchnikoff suggested the use of lanolin ointments containing 25% of white precipitate, calomel, or mercurio-salicyl arsenate.

Suspicious cracks or hangnails should have this ointment well rubbed in:—Calomel 33, soft paraffin 10, wool fat 57

Calomel ointment 30% used as a prophylactic for syphilis in rabbits, proved innocuous up to 8 hours after inoculation with the disease. Death from mercurial poisoning produced by single application of a large amount of the ointment — Nichols and J. Walker, *per J trop Med (Hyg)*, June, 1923, 223**Chologen** (*Rosenberg, Berlin, Yarrow, London*) No. 1 tablets contain calomel 0.05 g., podophyllin 0.005 g., No. 2 contain calomel 0.005 g., No. 3 contain calomel 0.005 g., podophyllin 0.005 g., camphor 0.0025 g., menthol 0.0025 g. course of treatment lasting for 60 days (No. 1 for 10 days; Nos. 1 and 2 for 10 days; No. 3 for 10 days) should be taken 2 or 3 times yearly. Cholelithiasis**2 81) Hydrargyri Succinimidum (U.S.P. XI) *Syn.* IMIDO-ACCINATE OF MERCURY**  $[C_2H_4(CO)_2N]_2Hg = 396.7$ *Dose.*—By injection,  $\frac{1}{4}$  to  $\frac{1}{2}$  grain (0.016 to 0.02 g.).

Mercury succinimide is a white powder, soluble in water about in 28. Hypodermically in syphilis has been used in 2½% solution. Addition of cocaine nitrate diminishes pain

**Hydrargyri Sulphidum Rubrum.** *Syn.* VERMILION, CINNABAR, CHINESE-RED.  $HgS = 232.7$ . Brilliant red powder insoluble in water and dilute acids prepared by subliming a mixture of mercury and sulphur. Both this and the black variety, **Hydrargyri Sulphuretum cum Sulphure** (*syn.* HYDRARGYRUM SULPHIDUM NIGRUM, ETHIOPIA'S MINERAL), of same composition are now rarely employed therapeutically**Unguentum Hydrargyri Bisulphidi (L.H.) *Syn.* UNGUENTUM CINNABAR SULPHURIS**

Mercuric sulphide 4 gr., precipitated sulphur 15 gr., yellow soft paraffin to 1 oz

**1 81) Æthiops Antimonialis.** A mixture of equal parts of black mercuric sulphide and grey antimony sulphide**Hydrargyri Persulphas. *Syn.* MERCURIC SULPHATE, HYDRARGYRI SUI PHAS.**  $HgSO_4 = 296.7$ .*Dose* — 2 to 5 grains (0.12 to 0.3 g.)A white powder made by dissolving mercury in boiling strong sulphuric acid. Water decomposes it with formation of yellow turpeth mineral, Hydrargyri Subsulphas (*Fr. Cx.*) or mercuric kysulphate,  $HgSO_4 \cdot 2HgO = 729.9$ 

It is a prompt emetic in dose of 2 to 5 grains which was given to children in croup and diphtheria to expel false membrane. It does not produce purging. Turpeth mineral ointment, Bazin's ointment, is 1 in 30 of benzonated lard. Used for ringworm and eporrhœa capitis

**Mercurous Sulphate,  $Hg_2SO_4 = 497.3$** 

A whitish crystalline powder slightly soluble in water and in dilute nitric acid. This salt, as also mercuric sulphate mixed with potassium bisulphate, is used for construction of electrical cells

**1) Hydrargyri Thiocyanas. *Syn.* HYDRARGYRI SULPHOCYANIDUM, MERCURIC THIOCYANIDE**  $Hg(CNS)_2 = 316.7$ .

White powder slightly soluble in water. Swells up on burning, producing PHARAOH'S SERPENTS "

[P2 81] **Hydrargyri Tannas** (B.P.C.).

*Dose.*—1 to 2 grains (0.06 to 0.12 g.), in pills or tablets, often with opium to prevent diarrhoea.

In brownish-green powder or scales containing 40 to 50% of Hg. Has been used in syphilis

[P1 81 84] **Merbaphenum** (U.S.P. XI). *Prop Name.* NOVASUROI (Bayer Products, London).

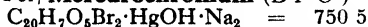
*Average dose* —2½ gr by hypodermic injection Is usually given intravenously or intramuscularly as a 10% solution

A double salt of sodium mercurichlorphenylquxyacetate with barbitone. A white crystalline powder containing about 34% of Hg

**Soluble** in water giving an alkaline solution

**Uses.** Causes profuse and rapid diuresis, especially in cardiac dropsy, but liable to produce toxic symptoms and superseded now by mersalyl.

[P2 81] **Mercurophen** (Sharp & Dohme, London) Sodium oxymercuri ortho-nitro phenolate. A germicide containing about 50% of mercury

[P2 81] **Mercurochromum** (B.P.C.)

*Syn and Prop. Names* MERCUROCHROME-220 SOLUBLE, DI-SODIUM DIBROMOHYDROXYMERCURI-FLUORESCIN, MERCUCROCOL (Evans, Sons, Lescher & Webb, Liverpool), MERCUCROME (Martindale, London), PIANOCROME (Pharmaceutical Specialities (May & Baker) Ltd, London)

It is patented in U.S.A. and in some other countries but not in England, and "Mercurochrome" is a trade mark in U.S.A. and some other countries, but not in England

*Dose* —By intravenous injection 0.002 to 0.005 g. per kilo, i.e., 0.13 to 0.32 g. per 10 stone (63½ kilo) man, preferably in 0.5% or greater dilution

Orally, up to 5 grains (0.3 g.) has been given thrice daily without toxic effects

Iridescent green scales giving a red solution which shows a green fluorescence when dilute. It contains 25 to 28% of Hg

The B.P.C. requires mercurochrome when used for intravenous injection to comply with a biological test to ensure that its toxicity is not greater than that of a standard sample of mercurochrome kept by the Pharmaceutical Society of Great Britain. (See Vol II)

**Soluble** readily in water, 1 in 185 of dehydrated alcohol, 1 in 65 of alcohol 90%. Insoluble in acetone, but soluble in a mixture of acetone and diluted alcohol. Insoluble in chloroform and ether. *Solutions should not be boiled or autoclaved.*

**Incompatible** with acids, alkaloidal salts, and with most local anæsthetics.

**Uses.** Mercurochrome has been extensively advocated as an antiseptic but most recent experiments show that, *in vitro*, its action is relatively weak. Intravenously in septicæmic conditions it is now regarded as of little value, and mercurial poisoning may

result. As a vesical injection in cystitis, pyelitis, and in gonorrhœa the 1% solution is used.

As a non-irritant antiseptic for local use a solution of mercurochrome 2 in water 35, alcohol 95% 55 and acetone 10 is employed.

Two cases of paralysis following mercurochrome intravenously (0.4% solution)—W. More, *Brit. med. J.*, 11/1934, 1045

#### **Bactericidal Action.**

Added to human defibrinated blood outside the body it in no way enhances the bactericidal power of the blood, injected intravenously it does not increase the bactericidal action tested shortly afterwards, and no special antiseptic properties are conferred on the bile by such injection—L. Colebrook and R. Hare, per *Lancet*, 1/1927, 1195

Lethal concentration of iodine against *S. aureus* about 1 in 10,000—mercurochrome 1 in 10,000,000—roughly 1000 times stronger—R. B. Blair, *Brit. med. J.*, 11/1930, 194

In blood mercurochrome is a very weak germicide—L. P. Garrod, *Brit. med. J.*, 1/1931, 268

**References to Treatment with Mercurochrome.** (For references prior to 1930 to the use of mercurochrome in a wide range of conditions, see 20th Edn.)

**BURNS.** Preferable to tannic acid (comparison of 2696 cases). It is an effective antiseptic in the presence of protein, the crust formed is thin and transparent, bed linen is not destroyed, it is non-irritant to tissues, a 2% aqueous solution is stable indefinitely, epithelisation under the scab is rapid. No general anaesthetic is given, all dead tissue is stripped off and the denuded area swabbed with normal saline and then with 2% aqueous solution of mercurochrome, the surface is then dried with an electric drier. On the first day 4 applications are given, on the second, 3, and on the third, 2. The area is dried off after each application and is always kept exposed to the atmosphere—A. C. Turner, *Brit. med. J.*, 11/1935, 995

**CHRONIC CERVICITIS.** Responded well when treated with a douche or paint.—L. C. Rivett, *Brit. med. J.*, 11/1930, 866

Discussion on value at meeting of Roy. Soc. Med. Apart from local application in chronic cervicitis, intravenously in appendix abscess, and irrigation in cystitis, the feeling of the meeting was apathetic rather than laudatory—*Lancet*, 11/1930, 1088

In cervical discharges (other than gonorrhœa) apply a 10% solution to the cervix on a swab and leave in place, paint the vagina with the same solution—Colonel L. W. Harrison, *Lancet*, 1/1932, 452.

**CYSTITIS.** Intractable cystitis with frequent micturition and pyuria well treated, especially amongst women—K. W. Heritage, *Brit. med. J.*, 11/1930, 866

**CONJUNCTIVITIS.** Painted on both lids at once it cuts short duration. Invaluable in chronic cases. Superior to silver, is less irritating and cannot damage cornea. Two paintings a week. PARINAUD'S CONJUNCTIVITIS cleared up. Maternity Department of Bristol Royal Infirmary issues 1% solution instead of silver for the eyes of new-born babies. Decrease of ophthalmia neonatorum. CORNIAL ULCERS can be painted with benefit. BOPHRARITIS benefited by painting. In ophthalmic surgery 1% is painted over the skin of the eyelids—E. R. Chambers, *Brit. med. J.*, 11/1930, 992

Parinaud's conjunctivitis cleared up in 2 weeks by drops, also useful in tuberculous conjunctivitis and in chronic dacryocystitis—J. Cole Marshall, *Brit. med. J.*, 11/1930, 1102

**GNORRHŒA.** Daily application of a 1% solution to the cervix and vagina, preceded by warm saline douche and swabbing, a very rapid and easy method of curing gonorrhœa in women, and keeps complications at a very low percentage 100% of cures in 158 cases.—R. S. Statham, *Brit. med. J.*, 1/1934, 607

For the inflamed urethra in gonorrhœa the ideal antiseptic is not yet found, mercurochrome is penetrating, irritating, and disappointing—H. D. L. Spence, *Lancet*, 1/1930, 19.

**OBSTETRICS.** Induction of labour by 0.5% mercurochrome in glycerin through a catheter into the uterus. Succeeded in about 66% cases. In uterine sepsis 1%



by intrauterine injection almost invariably cures.—R. Kelson Ford, *Brit. med. J.*, ii/1930, 727.

**OTORRŒIA.** In the subacute stage a 1% solution often acts like a charm, but should not be used for more than a fortnight as it is a definite tissue poison.—E. Watson-Williams, *Brit. med. J.*, ii/1933, 49.

**PNEUMONIA.** Mercuric chloride and mercurochrome intravenously retained as a desperate last throw.—P. H. Mitchiner, *Lancet*, i/1931, 350.

**RHEUMATISM, ARTICULAR.** Aspiration of an arthritic knee joint and injection of 1% mercurochrome in glycerin cleared up.—R. Kelson Ford, *Brit. med. J.*, ii/1930, 727.

**SEPTICÆMIA.** In puerperal sepsis (e.g., a hæmolytic streptococcus), intravenously disappointing, but more hope if infection due to *B. coli*.—L. C. Rivett, *Brit. med. J.*, ii/1930, 866.

10 to 15 ml. of a 0.5% solution intravenously on alternate or even successive days—successes recorded. Dangers are thrombosis and renal insufficiency.—Sir Thomas Horder, *Brit. med. J.*, ii/1931, 593.

No direct germicidal action by intravenous injection is possible. In septicæmia more harm than good.—P. H. Mitchiner, *Brit. med. J.*, i/1931, 267.

Though far from being an ideal blood antiseptic, it is perhaps the nearest approach that we at present possess.—Sir Thomas Horder, *Lancet*, i/1932, 171.

[P2 81] **Meroxyl** (Hynson, Westcott & Dunning, Baltimore)

A mixture containing approx. 50% of the sodium salt of 2,4-dihydroxy-3:5-dihydroxymercuri-benzophenone-2'-sulphonic acid with ammonium 2,4-dihydroxy-benzophenone-2-sulphonate, sodium acetate and water

For wet dressings and irrigation of wound 0.1% solution For urinary affections 0.5% solution.

[P2 81] **Metaphen** (Abbott, Chicago, Pharmaceutical Products, London)

The anhydride of 4-nitro-5-hydroxymercuri-*o*-cresol, a relatively non-irritating germicide. It is dissolved in water with the aid of sodium hydroxide which forms a sodium salt.

For use on infected areas, skin sterilisation and instruments and hands, and in wounds and open cuts, also for instillation in gonorrhœa, and in ophthalmology. Stated to be 11 times more potent than mercuric chloride. Usually employed in 1 in 5000 solution, though up to 1 in 1000 may be used.

**IMPETIGO CONTAGIOSA.** Thoroughly cleanse skin round infected area and paint the lesion with several layers of Metaphen in flexible collodion 1:5000 which is permitted to dry layer by layer. In 24 hours the easily removable layers are removed, the adherent part is left on and the mixture reapplied in several layers: repeat procedure on third day. On the 4th day all the Metaphen-collodion preparation is removed with the underlying incrustation. If the underlying skin is dry apply 2% ammoniated mercury ointment, but if still moist repeat the Metaphen-collodion treatment for another 3 days. Over 200 cases treated with success.—L. Hollander and J. J. Hecht, *Amer. J. Dis. Childh.*, Aug, 1934, 269.

[P2 81] **Neptal** (Pharmaceutical Specialities (May & Baker) Ltd., London)

*o*-Hydroxymercuripropionamidocarbonylphenoxycetic acid. A mercurial diuretic used in nephritis, œdema of cardiac or renal origin, and in pleural or pericardial effusions. It is stated to be free from toxicity in therapeutic doses, and to have rapid and prolonged action. Ampoules of 1 ml. contain 0.092 g. of active product with 5% theophylline.

*Dose.*—0.8 to 1.5 ml. intramuscularly daily or every other day, or, in urgent cases, the same dose intravenously diluted to 10 ml. with normal saline.

[P2 81] **Neptal Suppositories** contain Neptal 0.5 g., theophylline 0.25 g.

[P2 81] **Novurit** (Chimoin A.G., Budapest, Martindale, London). Sodium salt of hydroxymercuric allylamido-methoxytrimethylcyclopentane-bicarbonate.

Suppositories contain 0.5 g. of Novurit, ampoules contain 0.1 g. with 0.05 g. theophylline in 1 ml. *Dose.*—1 to 3 intramuscular or intravenous injections a week, commencing with a dose of 0.5 to 1 ml. and increasing to 2 ml.; suppositories, 1 or 2 a week. In cardiac œdema, ascites, hepatic cirrhosis, cardiorenal œdema.

Ten cases of congestive heart failure with œdema have been treated with this suppository and also with Novurit intravenously and with Salyrgan intravenously. The average twenty-four hours' excretion of urine per dose was for the suppository 87.2 oz., for Novurit intravenously 121.1 oz., for Salyrgan intravenously 91.8 oz. The previous administration of ammonium chloride results in an

increased diuresis. With the suppositories 68·7% of the diuresis occurred within the first twelve hours, while the corresponding figure for Salyrgan intravenously was 81·7%. The diuresis does not extend beyond twenty-four hours. No toxic or irritative effects of the suppository have so far been detected. It is concluded that Novumt suppository is an effective and safe diuretic.—J. Parkinson and W. A. R. Thomson, *Lancet*, i/1936, 16.

[P2 81] **Mersalylum** (*B.P. Add.*).

( $\text{HgOH})\text{CH}_2\cdot\text{CH}(\text{OCH}_3)\text{CH}_2\cdot\text{NHCO C}_6\text{H}_4\cdot\text{O}\cdot\text{CH}_2\cdot\text{COONa} = 505\cdot7$ . *Syn. and Prop. Name.* MERCURGAN, SODIUM SALICYL-( $\gamma$ -HYDROXYMERCURI- $\beta$ -METHOXYPROPYL) AMIDE-O-ACETATE, SALYRGAN (*Bayer Products, London*) (available only in 10% solution for injection).

*Dose.*—No dose is given in *B.P. Add.*, which states that for injections the official *Injectio Mersalyli* should be used.

White deliquescent powder containing 38·5 to 40·5% of Hg calculated on the dried substance.

**Soluble** 1 in 1 of water, 1 in 3 of alcohol 95%, 1 in 2 of methyl alcohol; insoluble in ether and chloroform. Aqueous solutions containing sodium chloride or other salts decompose with formation of toxic compounds except in the presence of some substance such as theophylline, which inhibits decomposition.

[P2 81] **Injectio Mersalyli** (*B.P. Add.*).

*Dose.*—8 to 30 minims (0·5 to 2 ml.) by intramuscular or intravenous injection. The smaller dose is given to test tolerance. It is usually given intravenously.

Mersalyl 10 g., theophylline 5 g., in sterilised water to 100 ml with sodium hydroxide *q.s.* to give a pH of about 7·8.

**Uses.** Chiefly used as a diuretic in ascites and œdema of cardiac and cardio-renal origin, and in ascites resulting from cirrhosis of the liver.

**Contraindicated** in acute disease of the kidneys and advanced nephritis.

Intravenous route gives better and quicker response. Diuresis begins in 1 to 4 hours and is complete in 8 to 12 hours; best given in the morning. Ammonium chloride, 8 to 15 g. daily for 3 or 4 days before injection, improves response.—G. W. Collins, per *Prescriber*, 1929, 71.

In preference 2 ml is diluted with 10 ml of saline and given slowly intravenously. In œdema of renal origin with blood pressure and blood urea normal the preparation is useful and probably safe.—Izod Bennett, *Brit. med J.*, ii/1930, 1047.

Severe toxic effects from intravenous injection of doses larger than stated *antea*.—C. T. Andrews, *Lancet*, ii/1931, 132.

As diuretic used in 60 cases.—*Brit. med J. Epit.*, i/1931, 65.

Found to rank second in importance to digitalis in treatment of heart failure. Not only causes diuresis but frequently a considerable diminution in frequency of attacks in cardiac asthma. No evidence of renal damage.—H. T. Hyman and N. M. Fenichel, per *Lancet*, ii/1932, 139.

**CARDIAC ŒDEMA.**—Salyrgan can be used without interruption and without fear of toxic effects. In one case a total of 270 injections was given over 5 years. Beneficial not only in relief of œdema but in staving off symptoms of early cardiac insufficiency.—I. M. Dixon, *New Engl. J. Med.*, i/1934, 800.

**HYDRASTIS***B.P.C., P. Helv. V.**Syn.* GOLDEN SEAL, YELLOW ROOT.*Dose* — 10 to 30 grains (0.6 to 2 g.)

The dried rhizome and rootlets of *Hydrastis canadensis* (Ranunculaceæ) *P. Helv. V.* requires 2.5% of hydrastine.

**Uses.** *Internally* it has tonic properties, acting as a bitter, and has been used in intermittent fevers. The drug and its alkaloids cause uterine contraction and are remedies in menorrhagia and dysmenorrhœa.

*Externally* in chronic inflammation of the mucous membrane, also for cracks and fissures of the nipple. It stimulates ulcers, and as a lotion (1 in 20 of liquid extract) checks profuse sweating and may be employed in acne and seborrhœa. In gonorrhœa, injection of a 1% solution of the liquid extract is of value.

**Extractum Hydrastis Liquidum (B.P.C.)**

*Dose.*—5 to 15 minims (0.3 to 1 ml.) Contains 2% of hydrastine. Large doses, 30 m. twice daily, have been given with success in chronic constipation with hypochlorhydria.

**Extractum Hydrastis (B.P.C.)** *Syn.* HYDRASTIN

*Dose* —  $\frac{1}{2}$  to 2 grains (0.03 to 0.12 g.). A dry alcoholic extract containing 8% of hydrastine.

Aperient, cholagogue, stomachic, and tonic, 3 to 6 grains in a pill, followed by effervescing sodium sulphate, is a useful biliary stimulant.

**[P. 81] Mistura Hydrastis et Ergotæ.**

Liquid extracts of hydrastis and ergot of each 30 m., chloroform water to 1 oz for a dose.

One of the most powerful remedies for menorrhagia.

**Tinctura Hydrastis (B.P.C.)**

*Dose.*— $\frac{1}{2}$  to 1 drachm (2 to 4 ml.)

Prepared with 10% of the liquid extract in alcohol 60%.

*Fr. Cx.* has 1 in 5 of the root by weight. Not standardised.

**Liquor Sedans** (*Parke, Davis, London*) *Dose* —  $\frac{1}{2}$  to 1 drachm (2 to 4 ml.)  
A specialty stated to contain in 1 oz hydrastine representing fluid extract of hydrastis 30 m., black haw (*Viburnum prunifolium*) 60 gr., Jamaica dogwood (*Piscidia piscipula*) 30 gr., with aromatics.

As ovarian and uterine sedative, for dysmenorrhœa, threatened miscarriage, etc.

**Hydrastina (Fr. Cx.).**  $C_{21}H_{21}O_6N = 383.2$ .

*Dose.*— $\frac{1}{2}$  to 1 grain (0.016 to 0.06 g.). *Fr. Cx.* has max single dose  $1\frac{1}{2}$  grains, max. during 24 hours  $4\frac{1}{2}$  grains approx.

An alkaloid in white prismatic crystals, slightly soluble in water, but soluble 1 in 120 of alcohol 90%, 1 in 2 of chloroform and 1 in 83 of ether; taste very bitter. Must be distinguished from extract of hydrastis, sometimes called hydrastin.

**Hydrastinæ Hydrochloridum (B.P.C.).**  $C_{21}H_{21}O_6N.HCl = 419.6$ .

**Dose** —  $\frac{1}{4}$  to 1 grain (0.016 to 0.06 g.) orally, or hypodermically as a 10% solution.

A crystalline soluble salt, constricts peripheral vessels and said to cause uterine contraction and arrest hæmorrhage

[P 81] **Tablets, Hydrastine Compound.** Hydrastine hydrochloride  $\frac{1}{4}$  gr, ergotin  $\frac{1}{2}$  gr, cannabin tannate  $\frac{1}{2}$  gr Efficient in checking menorrhagia and post-partum hæmorrhage.

**Hydrastinina.**  $C_{11}H_{13}O_3N$ . **Dose.** —  $\frac{1}{4}$  to  $\frac{1}{2}$  grain (0.016 to 0.03 g) increased up to 1 grain (0.06 g). Is obtained by the oxidation of hydrastine. In white or faintly yellow crystals soluble in alcohol, ether and chloroform, moderately soluble in hot water

**Hydrastininae Hydrochloridum** (B P C, Fr. Cx, P Ital V, P.G VI, P. Helv, P. Dan, P Belg IV).

$C_{11}H_{12}O_2NCl = 225.6$

**Dose** —  $\frac{1}{4}$  to  $\frac{1}{2}$  grain (0.016 to 0.03 g) hypodermically. Orally the dose may be increased up to 1 grain (0.06 g). Fr Cx. has max single dose  $\frac{3}{4}$  grain, max during 24 hours  $2\frac{1}{2}$  grains approx. P Belg IV and P. Helv V have approx  $\frac{1}{2}$  and  $1\frac{1}{2}$  grains respectively

In pale citron yellow crystals, soluble 1 in 1 of water. Has been used for internal hæmorrhage hypodermically

Useful in menorrhagia and dysmenorrhœa

**Beberinæ Sulphas** (B P C) Syn BEBERINE, BUXINE or PFIOSINE SULPHATE. **Dose** — 1 to 5 grains (0.06 to 0.3 g)

A mixture of alkaloidal sulphates with various impurities obtained from nectandra (bebeeru) bark, the stem bark of *Nectandra Rodiei* (Lauraceæ). It occurs in bitter translucent scales containing about 30% of beberine. Soluble 1 in about 1 of water, sparingly soluble in alcohol. Antipyretic and tonic similar to quinine, useful in menorrhagia

**Beberine Hydrochloride** is also occasionally used. In reddish-brown scales

**Berberidis Cortex** (B P C) is the dried bark of the stem of *B vulgaris*, and has been administered as Tinctura Berberidis Corticis (1 in 10), dose —  $\frac{1}{4}$  to 1 drachm, or as a decoction (1 in 20) or infusion (1 in 20)

**Berberinæ Sulphas** (B P C) Syn BERBERINE (or BERBERINIUM) ACID SULPHATE  $C_{20}H_{18}O_4N(HSO_4) = 433.2$

**Dose.** — 1 to 5 grains (0.06 to 0.3 g)

The acid sulphate of berberine, an alkaloid present in hydrastis and calumba but obtained mainly from *B vulgaris*. In bright yellow acicular crystals or as a dark yellow powder with bitter taste

**Soluble** 1 in 150 of water and in alcohol (90%)

**Uses.** Has been given for indigestion, diarrhœa, malaria, and sickness in pregnancy. Is administered by injection in oriental sore

Berberine sulphate in water said to be effective in oriental sore. Inject into the sore, and repeat after a week — R L Varma, *Indian med Gaz*, 1927, 62, 84.  $\frac{1}{4}$  grain of the sulphate in 1.5 ml of water. Hypertonic and isotonic saline strongly recommended in conjunction. Better than tartar emetic intravenously — P. V Karamchandani, *Lancet*, 1/1930, 78

Successful treatment of oriental sore with 3 ml of 2% berberine acid sulphate. Two to four injections effected a cure in 6 cases — *Prescriber*, 1931, 355

Berberine acid sulphate is of undoubted value in cutaneous leishmaniasis. 1 or 2 ml of a 1 per cent aqueous solution is infiltrated by means of a fine needle into the margins of the lesion. Four or five punctures are made and the infiltration

is evenly spread. The injections are given once a week, the part being kept covered. Three treatments is frequently sufficient; occasionally a large number is necessary.—R. N. Chopra, B. B. Didshit, and J. G. Chowlan, *Indian med Gaz.*, 1932, 194.

Analysis of treatment of over 300 cases. All those who received 5 or more injections (132) were definitely cured. If persevered with, the injections are a certain cure for oriental and possibly other sores.—E. W. Hayward, *Indian med. Gaz.*, May, 1933.

**Orisol** (*Pharmaceutical Specialities (May & Baker) Ltd., London*). Berberine acid sulphate in 2% solution for injection in the treatment of oriental sore.

*Dose*.—0.5 to 1.5 ml. is infiltrated round the edge of the sore and the procedure repeated at the end of a week.

**Berberina**,  $C_{19}H_{19}O_4N$ , crystallises in yellow needles with m.p. about  $144^\circ$ .

**Berberinæ Carbonas**,  $C_{19}H_{19}O_4N(HCO_2)$ ,  $2H_2O$ . Yellowish-brown crystals soluble in hot water and in alcohol; insoluble in cold water.

**Berberinæ Hydrochloridum** is the neutral salt,  $C_{19}H_{19}O_4NCl \cdot 2H_2O$ , occurring in bright yellow crystals soluble in water about 1 in 400.

**Berberinæ Phosphas** is the acid phosphate,  $C_{19}H_{19}O_4N(H_2PO_4) \cdot H_3PO_4 \cdot 1\frac{1}{2}H_2O$ . Bright yellow crystals soluble 1 in 15 of water.

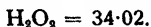
**Berberis** (*B.P.C.*) The dried stem of *B. aristata* (*Berberidaceæ*). A bitter tonic used in intermittent fevers. An extract from various species, combined with opium, is used in India as a local application in affections of the eye.

*Liquor Conc., I.C. Add.*, 1900. *Dose*.— $\frac{1}{2}$  to 1 drachm. Alcohol 20%, 1 in 2.

**Tinctura Berberidis** (*B.P.C.*) *Dose*.— $\frac{1}{2}$  to 1 drachm (2 to 4 ml.) 1 in 10.

Berberis berries (*Baies*) are official in *Fr. Cx.* as ingredient in *Electuaire diascordium*.

## HYDROGENII PEROXIDUM



**Liquor Hydrogenii Peroxidi** (*B.P., U.S.P. XI*) *Syn* LIQUOR HYDROGENII DIOXIDI, HYDROGENIUM PEROXYDATUM DILUTUM (*P. Helv. V*).

*Dose*.— $\frac{1}{2}$  to 2 drachms (2 to 8 ml.).

May be prepared by the action of diluted sulphuric acid on barium peroxide in presence of water. A colourless liquid with harsh metallic taste.

1 ml. yields about 10 ml. of oxygen, equivalent to 2.5 to 3.5% *w/v* of  $H_2O_2$ . 20 and 100-volume strengths (the latter is *Hydrogenium peroxydatum concentratum P. Helv. V*) are also available. The 100-volume solution, which contains about 30% *w/v* of  $H_2O_2$ , is more stable than weaker solutions, and can conveniently be used for their preparation.

**Soluté officinale d'Eau Oxygénée** (*Fr. Cx.*) is a 12-volume solution.

**Incompatibility.** It readily decomposes, especially in contact with metallic oxides and readily oxidisable substances. Among the more important incompatibilities are alkalis, ammonia, arsenious salts, glycerin, hypophosphites, iodides, mercurous salts, phenol, potassium bromide, chlorinated soda and chlorine water.

Ether restrains decomposition and is used for making ozonic ether.

**Uses.** Internally is non-poisonous, and has been given for pertussis, flatulent dyspepsia and other affections, but now it is

mostly employed locally as an antiseptic not precipitated by albumin. It is useful for assisting in removing surgical dressings which adhere obstinately. It is valuable used *undiluted* as a pigment, or diluted 1 in 8 as a spray, for diphtheria, tonsillitis, hay fever, laryngeal tuberculosis, putrid bronchitis and non-syphilitic ozæna, and as an antiseptic mouth-wash or gargle. For tuberculous and syphilitic ulcers, gangrene, malignant pustule and for purulent discharges it is antiseptic. It is astringent, *e.g.*, in epistaxis, and styptic in removing polypi. May be used locally for inoperable uterine cancer, chilblains, lupus, favus and other skin affections, also in gonorrhœa (up to 10-volume strength) occasionally. Wasp and hornet stings are at once relieved. It is sometimes used as an eye lotion, undiluted, in gonorrhœal conjunctivitis, or diluted 1 in 10 in diphtheritic conjunctivitis.

The 10-volume solution, preferably diluted with an equal volume of water, may be used in otorrhœa and otitis. After syringing out with weak boric acid lotion, allow to remain in 15 minutes, syringe out again, and dry carefully. Neutralising hydrogen peroxide solution with calcium carbonate and filtering is said to obviate the pain caused by syringing wounds in the ear with the ordinary acid preparation. This, of course, must be done only at the time of use as the neutral solution rapidly loses its strength.

The 20-volume strength can be used for acute or chronic and gouty periodontitis by syringing out pockets around affected teeth, and also for septic root canals.

Solution of hydrogen peroxide is also used for bleaching hair and fabrics.

Gangrene of scalp following use of a 30% solution of hydrogen peroxide for bleaching the hair—*Brit med. J. Epit*, 1/1926, 64.

**ACHLORHYDRIA** In about 75% of cases of achlorhydria the power of secreting acid can be restored by dieting, removal of septic foci and lavage of the stomach when fasting in the morning, with dilute hydrogen peroxide ( $\frac{1}{2}$  oz to the pint) to remove mucus. Treatment is continued daily until the washings are clear—A. F. Hurst, *Pharm J*, 11/1934, 675.

**OTITIS MEDIA.** Peroxide drops dangerous, and increased percentage of mastoid infections—Sir R. Woods. Its use should be abandoned in all cases—J. B. Hogan. Opposed to its use—H. Barwell—Discussion B.M.A. Ann. Meeting, 1933; *Brit med J*, 11/1933, 255.

**Dangers of hydrogen peroxide in treatment of otorrhœa** In contact with pus it yields a large quantity of oxygen which may cause serious symptoms and even death—*Prescriber*, 1926, 69.

**Collutorium Hydrogenii Peroxidi.** Hydrogen peroxide solution (20 volume) 500, oil of peppermint 1, elixir of saccharin 30, thymol water 470.

**Astringent Hydrogen Peroxide Mouth-Wash.** The above with 5% of solution of aluminium acetate added. *Dilute either of the above with 7 parts of water*. For painful ulcers of the mouth in syphilis.

**Gargarisma Hydrogenii Peroxidi.** Hydrogen peroxide solution 1 dr., sodium chloride 5 gr., glycerin 30 m., water to 1 oz.

**Guttæ Hydrogenii Peroxidi et Spiritus (St. T. H.)**

Hydrogen peroxide solution and industrial methylated spirit, equal parts. Used as ear drops

Best dispensed in separate bottles because on standing acetaldehyde and acetic acid are formed, and may cause irritation or a stinging sensation when used —W. A. Woodard and J. Pickles, *Quart. J. Pharm.*, 1934, 418

**Unguentum Hydrogenii Peroxidi.**

Hydrogen peroxide solution 10, anhydrous wool fat to 100 To be freshly made. Useful in eczema and other parasitic skin affections

**Ozonic Ether.**

*Dose* — $\frac{1}{2}$  to 1 drachm (2 to 4 ml)

Prepared by shaking a strong solution of hydrogen peroxide with ether and separating the ethereal layer. It yields 4 to 5 volumes of oxygen.

It is miscible with alcohol and with water in all proportions up to 3 times its volume. Is more stable than solution of hydrogen peroxide In conjunction with tincture of guaiacum, it is employed as a test for blood, *v* Vol. II Has been given internally for whooping cough.

**Solid Hydrogen Peroxide.** *Prop. Names* HYDROSOL (*Richter, London*), HYPEROL (*Berk, London*), PERHYDRIUM (*Merck, Darmstadt; Martindale, London*).

A solid compound of hydrogen peroxide and urea, stabilised with a trace of citric acid The compound contains about 35% of hydrogen peroxide and is stable below 60° A 10% solution is approximately the same strength as solution of hydrogen peroxide (10 volume)

Tablets contain 15 grains (1 g).

**Perhydrol** (*Merck, Darmstadt, Martindale, London*) 30% solution of hydrogen peroxide, yielding on dissociation 100 volumes of oxygen

**Calcii Peroxidum (B.P.C.)** *Syn.* CALCIUM SUPEROXYDUM, GORIT.  $\text{CaO}_2 = 72.08$  Crystals containing  $8\text{H}_2\text{O}$  are obtainable

*Dose.*—3 to 8 grains (0.2 to 0.5 g.) daily.

A white crystalline powder slightly soluble in water, evolving oxygen. It explodes if mixed with glycerin or formalin

A useful intestinal antiseptic, given in milk, for infants, *e.g.*, in summer diarrhoea. Recommended in hyperacidity, also in soil-contaminated wounds and in dentifrices

**Magnesii Peroxidum (B.P.C.)**  $\text{MgO}_2 = 56.32$

*Dose.*— $\frac{1}{2}$  to 1 drachm (2 to 4 g.).

A white tasteless powder insoluble in water, containing not less than 15% of  $\text{MgO}_2$  with magnesium oxide. Used where increased oxidation is desired, given for weak digestion, anæmia, and in diarrhoea of phthisis, vomiting, anorexia, flatulence and pyrosis 5 to 10% added to precipitated or prepared chalk powder makes a good dentifrice.

**Dentifricium Oxidans (R.D.H.)** Powdered hard soap 30 gr, powderedorris 30 gr, magnesium peroxide 1 dr, menthol 1 gr, oil of clove 2 m, precipitated chalk to 1 oz

**Magnocarbon** (*Richter, London*). Charcoal 4 gr, magnesium peroxide 4 gr, extract of belladonna  $\frac{1}{4}$  gr. *Dose* —1 or 2 tablets thrice daily. In hyperacidity, dyspepsia, flatulence and ulcer

**Perhydrol-Magnesium** (*Merck, Darmstadt, Martindale, London*) contains 25% of  $MgO_2$ . **Perhydrol-Zinc** is also supplied.

**Regyl** (*Bengué, London*) Tablets containing magnesium peroxide, sodium fluoride, pepsin, pancreatin and diastase *Dose*—1 tablet after meals. For auto-intoxication.

**Sodii Peroxidum.** *Syn.* SODIUM DIOXIDE, *FF VIII*, OXYLITH, "SOLID OXYGEN."  $Na_2O_2 = 77.99$ .

A yellowish white amorphous hygroscopic powder, dissolves in water with production of heat and evolution of oxygen 50% solution has been used in dentistry to whiten stained teeth Technically used as bleach for sponges, wool, bones, oils, etc

**Unguentum Sodii Peroxidi.** 20% in soft white paraffin may be tried with caution in acne.

**Zinci Peroxidum** (*Fr Cx Supp 1926, P Dan*)  $ZnO_2 = 97.38$  *Syn. and Prop Name* EKTOGAN (*Kirchoff and Neurath, Berlin*), DERMOTEN.

A white powder insoluble in water Used locally in skin affections Promotes healing of chronic ulcers For burns and wounds

**Incompatible** with corrosive sublimate 10% ointment or dusting powder is used

## HYOSCYAMUS

*B P, U S.P XI, P Helv. V, P Dan*

*Syn.* HYOSCYAMI FOLIA, HYOSCYAMUS LEAVES, JUSQUIAME (*Fr Cx.*), HENBANE LEAVES

[P1] "Alkaloids, the following, their salts, simple or complex — Atropine; Hyoscine; Hyoscyamine "

[81] "Alkaloids, the following, their salts, simple or complex.— Atropine except substances containing less than 0.15% of atropine, hyoscine except substances containing less than 0.15% of hyoscine, hyoscyamine except substances containing less than 0.15% of hyoscyamine "

*Dose.*—3 to 6 grains (0.2 to 0.4 g ) *U S P XI* average dose 3 grains. *P. Helv. V* has max. single dose 15 grains, max. in 24 hours 45 grains.

Hyoscyamus consists of the dried leaves and flowering tops of *Hyoscyamus niger* (Solanaceæ), it contains not less than 0.05% of alkaloids calculated as hyoscyamine. *U S P. XI* requires a minimum of 0.04% with not more than 25% of stems, none more than 7 mm. thick

**Uses.** Similar to those of belladonna and stramonium

Colocynth and other strong purgatives in pills are rendered less painful in action by addition of extract of hyoscyamus.

**Antidotes.** Treat as for poisoning by atropine, see p 228

[P1] **Extractum Hyoscyami Liquidum** (*B.P.*)

*Dose.*—3 to 6 minims (0.2 to 0.4 ml ).

Contains 0.05% of alkaloids calculated as hyoscyamine. 6 minims contain about  $\frac{3}{16}$  gr. of alkaloids.

[P1-81] **Extractum Hyoscyami Siccum** (*B.P.*). *Syn.* EXTRAC-TUM HYOSCYAMI



**Dose.**— $\frac{1}{4}$  to 1 grain (0.016 to 0.06 g.). The dose in the *B.P.* '14 was 2 to 8 gr.; the reduction was made to bring the dose of extract into line with that of other hyoscyamus preparations.

It is prepared by the same method as *Ext. Belladonnæ Siccum*. It conforms with *I.A.*, and is standardised to 0.3% of alkaloids. *P. Helv. V, P. Ital. V* and *F.E. VIII*, 0.5% of alkaloids; *P.G. VI* contains 0.5% of hyoscyamine.

[P1-81] **Extractum Hyoscyami** (*U.S.P. XI*). **Average dose.**— $\frac{1}{4}$  grain (0.05 g.)

In two forms, pilular and powdered; they contain 0.15% of alkaloids and are therefore about half the strength of the *B.P.* 1932 dry extract.

[P1-81] **Succus Hyoscyami** (*B.P.C.*), **dose**— $\frac{1}{2}$  to 1 drachm (2 to 4 ml.), is the juice expressed from fresh hyoscyamus and preserved with alcohol.

[P1] **Tinctura Hyoscyami** (*B.P.*)

**Dose.**— $\frac{1}{2}$  to 1 drachm (2 to 4 ml.). 1 drachm contains about  $\frac{1}{10}$  gr. of alkaloids.

Prepared with 10% *v/v* of liquid extract of hyoscyamus in alcohol 70%, and contains 0.005% *w/v* of alkaloids.

Some samples give a precipitate of green colouring matter on dilution with water.

[P1] **Tinctura Hyoscyami** (*U.S.P. XI*). **Average dose.**—30 minims (2 ml.)

Contains 0.004% of alkaloids and is therefore about four-fifths the strength of the *B.P.* tincture.

[P1] **Baume Tranquille** (*Fr. Cx*) *Syn* HUILE DE JUSQUIAME COMPOSÉE.

Macerate powdered leaves of belladonna, hyoscyamus, *Solanum nigrum*, poppy and stramonium, of each 50, with alcohol 200, and allow to stand 24 hours then add poppy seed oil 5000, warm for 6 hours at 60° to 70°, press and allow to deposit, and finally add oils of lavender, peppermint, rosemary and thyme, of each 1, and filter.

[P1] **Hyoscyami Semen** (*B.P.C.*) *Syn.* HENBANE SEED

The seeds of *H. niger*, containing about 0.05 to 0.1% of alkaloid, chiefly hyoscyamine, and 20% of oil.

[P1] **Meglin's Pills.** Hyoscyamus extract, valerian extract, and zinc oxide each 1 grain In sciatica

[P1] **Mictasol** (*Bengué, London*) Suppositories containing extract of hyoscyamus 0.05 g., Stovaine 0.01 g., ichthammol 0.25 g., malva purpurea 0.5 g For hæmorrhoids.

[P1-81] **Herba Hyoscyami mutici** (*P. Helv. V*). *Syn.* JUSQUIAME D'ÉGYPTE, EGYPTIAN HENBANE. From *H. muticus*, and contains not less than 0.8% of alkaloids, chiefly hyoscyamine. *P. Helv. V* permits it to be used for making standardised galenicals, but it must not be dispensed for hyoscyamus

[P1-81] **Hyoscyamina.**  $C_{17}H_{23}O_3N = 289.2$ .

**Dose.**— $\frac{1}{100}$  to  $\frac{1}{10}$  grain (0.0003 to 0.0006 g.), in cases of mania increased to  $\frac{1}{10}$  or  $\frac{1}{5}$  grain, dissolved in water by means of diluted sulphuric acid, or in a pill.

An alkaloid obtained from various Solanaceous plants, *Hyoscyamus muticus* being the best source. It is the *lævo* isomer of atropine (which is *dl*-hyoscyamine) into which it can be converted by heating or by the action of alkali. It is in light, snow-white crystals, m.p. 108° to 109°.

**Soluble** 1 in 120 of water, freely in alcohol, chloroform and ether.

**Antidotes.** Treat as for poisoning by atropine, *see* p. 228.

**[P1-81] Hyoscyaminæ Hydrobromidum.**

$C_{17}H_{23}O_4N \cdot HBr = 370.1$ .

*Dose.*— $\frac{1}{80}$  to  $\frac{1}{100}$  grain (0.0003 to 0.0006 g.), increased.

In small white crystals, m.p.  $152^\circ$ , soluble about 2 in 1 of water, also soluble in alcohol 90%.

**[P1-81] Hyoscyaminæ Sulphas (B.P.C.).**

$(C_{17}H_{23}O_4N)_2 \cdot H_2SO_4 = 676.5$ .

*Dose.*— $\frac{1}{80}$  to  $\frac{1}{100}$  grain (0.0003 to 0.0006 g.), increased up to  $\frac{1}{10}$  grain (0.006 g.) in mania.

In small white granular deliquescent crystals, soluble 2 in 1 of water and about 1 in  $4\frac{1}{2}$  of alcohol 90%.

*Uses.* As a mydriatic it acts like atropine, but with greater intensity, while the duration of effect is about equal.

It removes the pain of neuralgia, and is given for mental excitement, e.g., delirium tremens. In mania  $\frac{1}{8}$  grain may be given hypodermically. Is useful for prevention of sea-sickness. Tablets or granules of  $\frac{1}{80}$  gr. may be taken occasionally a day or two beforehand, and for the first few days on board; hourly if required.

**[P1 81] Hyoscina.  $C_{17}H_{21}O_4N = 303.2$ . Syn SCOPOLAMINE.**

A thick syrupy alkaloid, contained in *Hyoscyamus niger*, different species of *Scopola*, *Datura alba*, the flowers of which yield 0.5%, and other solanaceous plants. It may be obtained from the mother liquors of the preparation of hyoscyamine.

*Antidotes.* Treat as for poisoning by atropine, see p. 228.

*Uses.* Hyoscine base is used as a mydriatic in oily solution or as an ointment. Mydriasis is quick in onset and of short duration. For the preparation of aqueous solutions and for oral and hypodermic use a water-soluble salt is used, usually the hydrobromide.

**[P1 81] Oleum Hyoscinae (R.L.O.H.).** Hyoscine 4 gr. dissolved in minimum amount of chloroform and mixed with castor oil at  $61^\circ$  to 1 oz. Causes a mydriasis which is certain, quick in onset and of short duration.

**[P1 81] Oleum Hyoscinae (P.Helv. V)** is 1% in arachis oil,

**[P1 81] Unguentum Hyoscinae (R.L.O.H.). Syn. UNGUENTUM SCOPOLAMINÆ.** Hyoscine 1 or 2 gr. dissolved in minimum amount of chloroform and mixed with yellow soft paraffin at  $61^\circ$  to 1 oz.

**[P1-81] Hyoscinae Hydrobromidum (B.P.).**

$C_{17}H_{21}O_4N \cdot HBr \cdot 3H_2O = 438.1$ . Syn. SCOPOLAMINÆ HYDROBROMIDUM (U.S.P. XI, P. Ned. V, P. Jap., P. Belg. IV, F.E. VIII, P. Dan., P. Ital. V). P. Helv. V has  $2H_2O$ .

*Dose.*— $\frac{1}{80}$  to  $\frac{1}{100}$  grain (0.0003 to 0.0006 g.). The dose may be increased to  $\frac{1}{8}$  grain. P.G. VI has maximum single dose 0.001 g., maximum daily dose 0.003 g. U.S.P. average dose  $\frac{1}{100}$  grain.

The hydrobromide of *l*-hyoscine. In white rhombic crystals, soluble 1 in 2 of water, 1 in 13 of alcohol 90%. Melts at  $194^\circ$  to  $196^\circ$  after drying at  $100^\circ$  (U.S.P. XI  $190^\circ$  to  $192^\circ$ ).

*Uses.* Produces prompt depression of the motor area of the brain, and acts as a powerful hypnotic; especially useful in acute mania and delirium, including delirium tremens, calming the excitement and rapidly inducing sleep. Occasionally a short stage of excitement precedes sleep and, in general, it is a less reliable

hypnotic than chloral hydrate or morphine. It is also useful in chorea, asthma and pertussis, and is employed in the intensive withdrawal treatment of morphine addiction (*see under Morphina*). Hyoscine hydrobromide is extensively used in the symptomatic treatment of paralysis agitans and post-encephalitic parkinsonism. Doses of  $\frac{1}{100}$  to  $\frac{1}{50}$  gr. thrice daily *per os* often greatly relieve the tremors and muscular rigidity. If pilocarpine is given simultaneously to prevent dryness of the mouth and paralysis of accommodation the dose can frequently be increased to  $\frac{1}{20}$  gr. and occasionally to  $\frac{1}{10}$  gr. thrice daily. In conjunction with morphine, hyoscine is used for the induction of "twilight sleep" in labour (*vide infra*). Hyoscine hydrobromide is also used as a mydriatic in 1% aqueous solution or as the eye ointment or lamella

**DELIRIUM TREMENS.** Hyoscine  $\frac{1}{10}$  gr with morphine  $\frac{1}{4}$  gr is a sheet anchor, but may be cumulative —W. Starkey, *Brit. med. J.*, 1/1920, 47

**ENCEPHALITIS, EPIDEMIC.** Hyoscine of undoubted value, though effect is temporary. Start with  $\frac{1}{100}$  grain once a day hypodermically, increased if necessary to  $\frac{1}{50}$  grain. *Per os* larger doses may be employed thrice daily, preferably after meals —P. K. McCowan and co-workers, *Brit. med. J.*, 1/1926, 779, *Lancet*, 1/1926, 802

**PARALYSIS AGITANS.** The medicament of choice. —W. Freeman, *J. Amer. med. Ass.*, 11/1927, 1320

Paralysis agitans treated. Give a mixture of hyoscine  $\frac{1}{100}$  gr with pilocarpine nitrate  $\frac{1}{8}$  gr and solution of strychnine hydrochloride 3 m 4 times daily, gradually increased until the tremor is controlled —A. F. Hurst, *Brit. med. J.*, 1/1926, 845

**POST-ENCEPHALITIC PARKINSONISM.** Hyoscine hydrobromide produces quite definite and even marked improvement —A. J. Hall, *Brit. med. J.*, 1/1926, 129

Chronic encephalitis treated with hyoscine hydrobromide  $\frac{1}{100}$  gr thrice daily, and with harmine —*Lancet*, 11/1929, 794

Marked relief in chronic cases of parkinsonism and disturbance of sleep, following continued administration of hyoscine hydrobromide  $\frac{1}{100}$  gr thrice daily by mouth, but not curative, and symptoms returned on suspension —A. G. Robb, *Brit. med. J.*, 11/1925, 646

[P1 81] **Guttæ Hyoscinae** (R.L.O.H.) 1 or 2 grains to 1 ounce

[P1] **Hauftus Hyoscinae** (Mid. H.).

Hyoscine hydrobromide  $\frac{1}{100}$  gr, compound tincture of lavender 5 m, chloroform water to 1 oz. For the sequelæ of encephalitis lethargica.

[P1 81] **Lamellæ** for ophthalmic use contain (R.L.O.H.)  $\frac{1}{800}$ ,  $\frac{1}{1000}$  or  $\frac{1}{2000}$  grain, also  $\frac{1}{500}$  grain.

[D P1 81] **Nebula Hyoscinae Composita** (B.P.C.). An aqueous spray containing hyoscine hydrobromide 0.057% w/v, cocaine hydrochloride about 0.9% w/v, and atropine sulphate about 0.1 w/v

[P1] **Oculentum Hyoscinae** (B.P.).

0.125% of hyoscine hydrobromide in simple eye ointment

### Scopolamine-Morphine Anæsthesia.

Hyoscine hydrobromide,  $\frac{1}{100}$  to  $\frac{1}{50}$  gr or more, and a salt of morphine  $\frac{1}{4}$  to  $\frac{1}{2}$  gr., are injected on the evening before the operation, and a similar or higher dose in the morning before the operation. This alone may suffice to produce deep sleep. If not, ether or chloroform may be given until complete anæsthesia occurs. Patients sleep for hours through the first painful periods after the operation

Morphine-scopolamine narcosis advocated for routine use as a preparation for surgical anaesthesia in children over one year of age. The solution, given hypodermically, contains 0.01 g. of morphine and 0.0005 mg. of scopolamine per ml. At 12 years the whole dose is injected, under 10, three-quarters, under 6, a half, under 4, a third; under 2, a quarter. Anaesthesia begun and consciousness regained with much less distress, and danger of syncope at onset reduced. Applied without ill-effect in over 800 children.—P. F. Armand-Delille, *Bull Acad Méd, Paris*, 1932, 890.

### The "Twilight Sleep" method of inducing child-birth

One of the physiological effects of scopolamine is to induce temporary loss of memory. The only successful method of inducing "Twilight Sleep" is to give doses according to needs. Hypodermic injection of morphine  $\frac{1}{8}$  to  $\frac{1}{4}$  gr. most commonly used. First dose of scopolamine  $\frac{1}{150}$  gr., at the end of 1 hour a second injection of  $\frac{1}{150}$  gr. is given—injecting at hourly intervals controlled by patient's condition. The number of the scopolamine injections matters little. *The morphine must not be repeated.* Marked absence of maternal shock afterwards. Child usually born with shallow respiration, but artificial respiration improves breathing. A little chloroform used in the late second stage, and when the head appears give  $\frac{1}{4}$  or  $\frac{1}{2}$  ml. of pituitary extract.—A. W. Bourne, *Clin. J.*, Dec 19, 1923, 601.

In the morphine-scopolamine method the child was born in 3% of cases oligopnoeic—of a blue colour with very shallow breathing. In each case it recovered spontaneously—morphine not necessarily the cause.—F. W. N. Haultain, *Brit med J.*, 1/1921, 341.

Specially indicated in primiparae. Chloroform only at very end of second stage. Postpartum haemorrhage not more frequent than usual.—N. Hirschman, *Brit med J.*, 11/1922, 669.

**Investigation of 32 cases by a Committee appointed by the Section of Obstetrics and Gynaecology of the R.S.M. in 1917.** The average number of injections of scopolamine was 4.5. Pituitary extract 0.25 ml. was given in 17 cases in the second stage. The average duration of labour after commencement of treatment was 5 hours 41 minutes in primiparae and 6 hours 5 minutes in multiparae. The injections caused lengthening of intervals between contractions, which were diminished in strength and duration. Voluntary expulsive efforts did not arise automatically. There was thirst in every case, and nausea in some. Some complained of pain in second stage. There was sleep between pains in every case. General anaesthesia was induced in 10 cases. One stillbirth resulted, most babies showed apnoea, and all were thirsty for 24 hours. Amnesia and not analgesia the aim. Amnesia was complete in 17 cases, incomplete in 12, and failed in 3. The treatment is good for the mother but needs unremitting attention from doctor and nurse. No danger with careful observation. The memory test is useless. Strict precautions must be taken to exclude all adventitious stimuli.—J. St. G. Wilson, *Med. Pr.*, 1927, 407. See also Gwathmey's *Synergistic Theory (Magnesium Sulphate and Morphine)*, p. 139.

Scopolamine-morphine narcosis in labour. In 25% of cases result very good, in 15% good, and in 10% no benefit.—J. S. Quin, *Lancet*, 1/1929, 668.

"Twilight Sleep" given as routine in hundreds of cases.—G. W. Theobald, *Brit med J.*, 11/1930, 664.

Three doses of hyoscine hydrobromide given hypodermically at  $\frac{1}{4}$ -hourly intervals when regular pains commence (in primiparae when cervix is three fingers dilated), and repeat every 2 hours as long as labour lasts. Up to  $\frac{1}{100}$  gr. used without ill effect. Chloroform given in second stage. Important not to omit last (third) injection, even if child about to be born. Excellent results and no ill effects on babies.—A. M. Claye, *Brit med. J.*, 11/1931, 12.

Hyoscine  $\frac{1}{150}$  gr. in 2 ml. of 50% magnesium sulphate solution adopted as routine as a reasonable analgesic in labour. Safe and fairly effective. One dose usually enough.—R. Kelson Ford, *Brit med J.*, 11/1930, 726.

An analysis of 50 cases of amnesia in labour using hyoscine hydrobromide alone. Entirely safe for mother and child. Labour not delayed, puerperal

morbidity not increased, and babies born without circulatory or respiratory defects: not suitable for domiciliary midwifery—T. Barnet, *Brit. med. J.*, 1/1934, 940.

[P1-81] **Genoscopamine** (*Amido Laboratories, Paris, Wilcox, Jozeau, London*). Nitrogen oxide of scopolamine in granules containing 0.5 mg. (dose—2 three times daily), drops (dose—20 drops = 1 mg. of Genoscopamine, three times daily), or ampoules of 1 ml (= 1 mg.) for subcutaneous injection. Has a therapeutic action similar to that of scopolamine but is less toxic.

[P1 81] **Vasano** (*Schering, London*). Camphoric acid salts of the mandragora bases (*l*-scopolamine and *l*-hyoscyamine). Dose—2 dragées each of 0.0075 gr. Prophylactic against travel sickness.

[P1 81] **Duboisine Sulphate**, dose— $\frac{1}{16}$  to  $\frac{1}{8}$  grain (0.00025 to 0.001 g.), is a mixture of alkaloidal sulphates from *Duboisia myoporoides* (Solanaceæ) consisting chiefly of hyoscyamine and hyoscyne sulphates. A deliquescent yellowish-white crystalline powder. Used as a mydriatic in solution (0.2 to 0.5%) or ointment.

[P1 81] **Guttæ Duboisinæ** (R.L.O.H.) Duboisine sulphate 1 gr., sterilised water to 1 oz.

[P1 81] **Dulcamara** (B.P.C.) *Syn.* WOODY NIGHTSHADE, BITTER-SWEET.

The dried stem and branches of *Solanum Dulcamara* (Solanaceæ). Sedative and analgesic. It has also been used in the treatment of scaly cutaneous eruptions.

[P1] **Infusum Dulcamaræ**. 1 in 10. Dose—1 to 2 ounces.

[P1] **Lactuca** (B.P.C.) *Syn.* LETTUCE, WILD LETTUCE.

The fresh flowering herb, *L. virosa* (Compositæ). Contains traces of a mydriatic alkaloid, possibly hyoscyamine.

[P1] **Extractum Lactucæ** (B.P.C.). Dose—5 to 15 grains (0.3 to 1 g.) A soft extract prepared from the fresh juice. A mild sedative for cough.

**Lactucarium**. *Syn.* LETTUCE OPIUM. Dose—5 to 15 grains (0.3 to 1 g.) The dried latex of lettuce. Brownish masses with opium-like odour and bitter taste, partly soluble in alcohol and in ether.

[P1 81] **Scopolia** (B.P.C.) *Syn.* SCOPOLA.

Dose.—1 to 2 grains (0.06 to 0.12 g.) The dried rhizome of *S. carmoli* (Solanaceæ).

Contains about 0.4% of alkaloids, chiefly hyoscyamine.

## ICHTHAMMOL

*Syn. and Prop. Names.* AMMONIUM ICHTHOSULPHONATE, AMMONIUM SULPHO-ICHTHYOLATE (*P. Ital. V, F.E. VIII*), AMMONIUM SULFOBITUMINOSUM (*P. Helv. V*), AMMONIUM BITHIOLICUM (*P. Belg. IV, P. Jap.*), ICHTHOSULPHOL, ICHTHYOL (*Österreichische Ichthyol-Gesellschaft, Seefeld in Tirol; Martindale, London*), ISAROL (*Ciba, London*), PERICHTHOL (*British Drug Houses, London*), SUBITOL (*C. Zimmermann, London*).

Dose.—5 to 10 grains (0.3 to 0.6 g.)

A viscous, brownish substance with a disagreeable odour, obtained by destructive distillation of fossil fish deposits.

It contains not less than 10·5% of organically combined sulphur, and sulphur as sulphates is not more than one-quarter of the total S. It contains not more than 50% of water.

**Soluble** in water; partly soluble in alcohol 90% and in ether; miscible with glycerin and fixed oils.

**Uses.** Internally has been given for rheumatism and skin affections, and as an intestinal antiseptic in constipation and dyspepsia. It also reduces expectoration and cough. Externally it is used in chronic skin diseases, as eczema, psoriasis and acne. Applied on wool as vaginal tampon, and used as pessaries and suppositories, and as injections 2 to 5%, in gonorrhœa, cystitis and vaginal discharges. Also applied to cracked nipples and erysipelas. In furunculosis it has been well spoken of. For pruritus and ulcers a 10% solution is used, and may be combined with lead and mercury without the formation of sulphides. For burns it may be used mixed with zinc oxide or bismuth (the powder being spread evenly over the surface), or in ointment (10 to 50%). In mumps the swelling and pain are said to be rapidly relieved by inunctions of equal parts of ichthammol and lanolin.

ALBUMINURIA is well treated by ichthammol internally combined with *B. coli* injections.—F. J. Sadler, *Lancet*, 1/1922, 930.

GONORRHOEA treated by intramuscular injection of 2% solution of ichthammol in doses of 3 ml. every second or third day—diluted just before injection—*Brit. med. J. Epit.*, 1/1926, 2.

**Collodium Ichthammolis (B.P.C.).** Ichthammol 1 in simple collodion *q.s.* to 8. Used for eczema, erysipelas and other skin diseases.

**Collodium Ichthammolis cum Æthere (B.P.C.).** Ichthammol 1 in ether and simple collodion *q.s.* to 4.

**Gelatinum Zinci et Ichthammolis (B.P.C.).** *Syn.* PASTA ZINCI ET ICHTHAMMOLIS, UNNA'S PASTE WITH ICHTHAMMOL.

Ichthammol about 2% in a basis of zinc oxide and glycerogelatin.

**Glycerinum Ichthammolis (B.P.C.).** Ichthammol 10% *w/w* in glycerin.

LYMPHANGITIS well treated with glycerin and ichthammol—H. W. Webber, *Brit. med. J.*, 1/1931, 206.

**Parogenum Ichthammolis (B.P.C.).** *Syn.* ICHTHAMMOL VASOLIMENT. 10% *w/v*.

**Mistura Ichthammolis.** *Dose*—1 to 3 drachms in water. Ichthammol 6, simple elixir 20, water 10.

**Oculentum Ichthammolis cum Zinci Oxido (Mid H.).**

Ichthammol 1, zinc oxide 15, yellow soft paraffin to 100. For chronic blepharitis.

**Pasta Ichthammolis (B.P.C.).** *Syn.* GELATINUM ICHTHAMMOL. Ichthammol 10% in a glycerogelatin basis.

**Pasta Ichthammolis et Olei Terebinthinæ.**

Ichthammol 1, oil of turpentine 1, mix. Of value in chilblains.

**Pessus Ichthammolis (B.P.C.)** contains 10 gr. (0·6 g.) in glycerin suppository basis to 120 gr. For leucorrhœa.

Ichthammol pessaries are sometimes required to be made with oil of theobroma basis. They are also made with resorcinol 3%, and these must be made with oil of theobroma.

**Pilula Ichthammolis.**

Ichthammol 2½ gr, compound tragacanth powder ½ gr, powdered liquorice 1½ gr. Make a pill on hot plate if necessary

**Suppositorium Ichthammolis (B.P.C.)** contains 3 grains of ichthammol in glycerin suppository basis.

Suppositories may contain 3 grains (0.2 g.) with a basis of theobroma 12 grains. The mixture must be almost "set" whilst pouring into the moulds, otherwise may separate. The addition of beeswax is not desirable, indeed a large proportion will render the suppository quite insoluble. Ichthammol pessaries or suppositories in a glycerogelatin base must not be overheated or they may become insoluble.

If a stiffer preparation is required than that obtained with glycerin suppository mass, the following proportions are satisfactory:—Ichthammol 10, glycerin 60, gelatin 16, water 14

Tampons may be prepared with 5, 10 or 20% of ichthammol in glycerin

**Unguentum Ichthammolis (B.P.C.)** 10% in wool-fat ointment

**Unguentum Ichthammolis Compositum (B.P.C.)** Ichthammol 9%, with sulphur, starch, resorcinol, betanaphthol and salicylic acid in wool-fat ointment.

**Unguentum Ichthammol et Zinci Oxidi (R.L.O.H.)** has ichthammol 8 gr., zinc oxide 15 gr., yellow soft paraffin to 1 oz.

**Ichthalbin** (Knoll, Ludwigshafen, Pharmaceutical Products, London). A combination of ichthammol and albumin, an odourless and tasteless brown powder. Used internally for eczema, nervous intestinal affections and during convalescence from fevers, in doses of ½ to 15 grains (0.05 to 1 g.)

**Ichthammol Resorcin** contains resorcin 10% for external use

**Ichthammol Salicyl** is a powder made with either 25, 33½ or 50% of sodium salicylate for psoriasis, acne rosacea and for rheumatic pains, and has been given internally in pills for tuberculosis.

**Lithium and Sodium Ichthammol**, dose of either —10 to 30 grains (0.6 to 2 g.) per diem, and **Zinc Ichthammol** for external use, are also prepared

**Ichthoform** (Cordes, Hermann, Hamburg) is a condensation product of ichthammol and formaldehyde for use as an intestinal antiseptic. Dose — 1½ to 5 grains (0.1 to 0.3 g.)

**Ichtholdine** (Sharp & Dohme, London). A preparation containing ichthyol, iodine, phenol, hydrastine hydrochloride, boroglyceride and eucalyptol. For treatment of chronic inflammatory conditions of the mucous membranes, e.g., endometritis, ulceration of the cervix and vagina, etc.

**Thigenol** (Hoffmann-La Roche, London) is the sodium salt of a synthetic sulpho-oleic acid, containing 2.85% of S. Soluble in water, glycerin, alcohol, miscible with fats and oils. A 5% ointment relieves eczema. Tampons and pessaries also available.

[P2] **Vaginoids** (Sharp & Dohme, London). Suppositories containing ichthyol 1½ gr., phenol 2 gr., iodine (combined) ½ gr., zinc phenolsulphonate 1 gr., in a glyco-gelatin basis. For ulcerations of the cervix and vaginal inflammations

**Sphagnol** (Peat Products, London). A native tar product produced from peaty deposits. In blepharitis, eczema, piles, sores and burns. Detergent and relieves insect bites in tropical countries. Ointment (10%), Medical Soap (15%), Toilet Soap (5%), Shaving Soap (5%) and Suppositories (3 gr., for piles) are made.

## INFUSA

Infusions are dilute solutions of the water-soluble extractives of vegetable drugs, prepared by macerating the drugs in hot or cold distilled water for a short period of time, usually 15 minutes, and then straining. Cold water must be used if the drugs contain an appreciable amount of starch. Infusions are chiefly used as vehicles for other drugs, and are consequently of either an aromatic or bitter nature.

The infusions in the *B.P.* and *B.P.C.* are of two types.—(a) freshly prepared infusions, and (b) infusions prepared by diluting concentrated preparations with 7 times their volume of distilled water.

### Fresh Infusions.

*These must be used within 12 hours of their preparation. If the prescriber wishes the fresh infusion to be dispensed, it must be specified on the prescription as "fresh" or "recens."*

### Concentrated Infusions.

These are weak alcoholic solutions obtained by double or triple maceration or percolation, with usually 25% alcohol. When diluted with 7 times their volume of distilled water they generally closely resemble the fresh infusions. Infusion of buchu, however, shows variation according to the method of preparation; the fresh infusion contains much more mucilage than one prepared by dilution from the concentrated preparation. Concentrated infusions of drugs such as digitalis and ergot are unstable, and only the fresh infusions should be used.

**Tisanes.** Infusions or teas (usual strength 1 in 10) of herbs are largely used by the laity in France, Italy, etc. Those mostly in use are—*Tilleul*, or lime flowers (*Tilia B.P.C.*), the dried inflorescences with their attached bracts of *Tilia europæa* and other species (anti-spasmodic, diaphoretic), senna and manna (largely used); *Queues de Cerise*, cherry-stalks (diaphoretic), peppermint, tamarinds; *Bourrache*, borage-leaf tea, chamomile; *Mauve*, *Malva sylvestris*, marshmallow flowers (demulcent); *Chiendent*, couch-grass (kidney tonic); aniseed (both varieties); linseed, *Orge* (pearl barley). A large number of other tisanes are prepared.

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## INSULINUM

### B P

[P1] "*Insulin*"

[87] *Medicines made up ready for the internal treatment of human ailments containing insulin must be labelled with the words "Caution. It is dangerous to take this preparation except under medical supervision" instead of the word "Poison"*

The original patent (Br. Patent No. 203,778) was taken out by F. G. Banting, J. B. Collip and C. H. Best in the name of Toronto



University, and the British rights were given to the Medical Research Council.

The Therapeutic Substances Act, 1925, and Regulations, 1931, control the manufacture under licence, standard, quality, containers, etc. Further Regulations, Part III, Sec. 9 (2), Aug. 1, 1931, provide for the addition of preservative to preparations like insulin, sealed in containers holding more than one dose.

The relation of the pancreas and diabetes was established by the experiments of Von Mering and Minkowski; extirpation of the pancreas in dogs was followed by persistent glycosuria. The pancreas consists of two types of tissue—the *acinar*, secreting the pancreatic juice (*external* secretion), which reaches the intestine through the pancreatic duct, and groups of cells, known as the “islands of Langerhans.” The latter show pathological changes in varying degree in most patients dying of diabetes mellitus.

The islands of Langerhans were proved to contain a substance which lowers the blood sugar, and diminishes or abolishes excretion of sugar in the urine of diabetic dogs. Subsequently, by extracting foetal or adult normal pancreas with alcohol, an extract was made which caused a lowering of blood sugar, and of the glucose in the urine, when injected into a boy suffering from the disease. The alcohol evidently prevented the destruction of the principle by the digestive ferments.

On injection, it converts glucose into the active form, and if given at proper intervals blood sugar is maintained at normal level, and the urine remains free of sugar. Fat is completely oxidised. Acetone bodies disappear from the urine and diabetic acidosis and coma are prevented—a restoration to normal metabolism.

**Distribution in Nature.** Insulin is present in potatoes, rice, beetroot and celery. A substance having an insulin-like action in reducing blood sugar has also been extracted from the kidney, spleen and muscle tissue of dogs and cattle.—C. H. Best and D. A. Scott, per *Prescriber*, 1924, 220.

An extract of yeast has an effect similar to insulin when tested on animals and diabetics.—Winter and Smuth, *Brit med. J.*, 1/1923, 711, 819.

Insulin may be obtained from the islet tissues of the cod, which probably contains about 10 times as much, weight for weight, as mammalian tissue—*Biochem. J.*, 1924, 18, 665.

It is now becoming generally recognised that no tissue, other than that of the pancreas itself, contains insulin that can be extracted by the methods now available. Best and his co-workers have developed improved methods and repeated much of the earlier work on the extraction of insulin from various substances. Not only have they failed to find any evidence of the presence of insulin-like substances in various vegetables, but they have failed to find any extractable insulin in the blood, liver, spleen, kidney or muscle. Consequently, when an extract which acts like insulin is obtained from a tissue other than the pancreas, it is reasonably certain that the tissue concerned must be of pancreatic origin.—M. H. Power, R. W. Cragg and M. C. Lindem, *Proc Mayo Clin.*, 1936, 101.

**Manufacture.** The method described in the *B.P.* involves the extraction of minced pancreas, which must be used fresh or kept frozen, with alcohol and hydrochloric acid. The filtrate is evaporated and treated with stronger alcohol, and the filtrate treated with dehydrated alcohol. The resulting precipitate is collected, dissolved in water and the active material separated by adjusting to the isoelectric point (which corresponds to a pH of

between 5 and 6), or by treatment with trinitrophenol (picric acid). In the former case, the precipitate is dried and powdered. In the *picrate method* used in Gt. Britain (Brit. Patent 216,978, M.R.C. and H. W. Dudley), the precipitate is dissolved in an acidified aqueous-alcohol solvent, the insulin re-precipitated by pouring into acetone, and the precipitate dried.

[P1-87] **Crystalline Insulin.** The first crystalline insulin was obtained by Abel (*Proc. nat. Acad. Sci.*, 1926, 12, 132) by precipitating impurities from crude insulin in weak acetic acid solution by means of brucine, and then precipitating the insulin by the addition of N/6 pyridine. A potency of 40 units per mg was claimed. Although other workers have claimed the isolation of crystals with activities very much greater than this—even up to 400 units per mg.—these results have not been confirmed. Culhane *et al.* (*Biochem. J.*, 1929, 397) found the activity of preparations obtained by Abel's and other methods to be 23 to 27 units per mg. Scott (*Biochem. J.*, 1934, 1532) showed that crystalline insulin contained zinc, and if electro dialysed to remove the metal it could not be crystallised. Crystallisation was found to be facilitated also by the presence of salts of other metals such as cadmium, nickel and cobalt. The ashes of crystalline insulins prepared with each of these metals contained a constant proportion of metal, and were proportional to the atomic weights of the metals each contained, thus indicating that the metal was in chemical combination in the crystals.

#### **Chemical Composition and Stability.**

The empirical formula obtained for Abel's crystalline insulin is  $C_{45}H_{75}O_{17}N_{11}$ . Values for the molecular weight vary from about 10,000 to 37,000 according to the method, most results being nearer the higher figure. Insulin obtained by precipitation at the isoelectric point is an amphoteric protein giving soluble salts with weak acids or alkalis. Strong acids precipitate the solutions and strong alkalis destroy the activity. It is most stable in acid solutions at low temperatures. Heating at 80° with 1% sodium chloride for 1 to 1½ hours causes coagulation. It is inactivated by proteolytic enzymes, *e.g.*, trypsin, pepsin or papain, hence the ineffectiveness of insulin *per os*.

Commercial insulin is composed of at least three substances: the true pancreatic hormone A, the anti-insulin B, and co-insulin C. A and B have been obtained in crystalline form—C. Funk, *Lancet*, 11/1926, 1244.

[P1-87] **Insulin in Solution (B.P.)** is obtained by dissolving the dry powder in water acidified to give a reaction between pH 3 and pH 4. The *B.P. Add.* requires that when insulin is prescribed, insulin in solution containing 20 units per ml. shall be dispensed unless some other strength, or insulin in tablets, is specified. It was originally required to contain an antiseptic at least as effective as 0.5% of phenol when distributed in containers holding more than one dose. The *B.P. Add.* makes the addition of an antiseptic optional, stating that "it is usual to add a sufficient proportion of some antiseptic to prevent the growth of any

organism which may be accidentally introduced in the process of removing a portion of the contents of the container."

Doubtful if antiseptic desirable—O Leyton and E. P. Poulton, *Lancet*, 1/1931, 996 T Izod Bennett, *ibid*, 1053 Compulsory addition injurious—F Sandor, *ibid*, 1422.

Solutions with pH 3 to 4 are themselves germicidal, but a slight increase of alkalinity destroys germicidal action and actually converts it into a culture medium if no preservative is present, the presence of the usual proportion of phenol suffices to keep it germicidal—P Hartley, *Lancet*, 11/1931, 584 Insulin and preservatives—*Prescriber*, 1931, 406.

While insulin alone in normal dosage has no effect on the size of the heart-beat of the rabbit, and in 16 times the normal dosage the size of the beat decreases only very slightly, solutions containing cresol or phenol in the concentration in which they are normally used as preservatives cause a marked decrease in the size of the heart-beat. The alleged slowing of the heart-beat by insulin is due to the preservative used in commercial insulin solutions—M. M O Barrie, *Quart. J Pharm*, 1936, 485

[P1 87] **Insulin in Tablet Form (B.P.)** is obtained by compressing the dry powder mixed with a neutral diluent

**Units.** A unit was originally taken as the amount of insulin which on subcutaneous injection can lower the percentage of blood sugar to 0.045 within 4 hours in a rabbit weighing about 2 kg from which food has been withheld for 16 to 24 hours. Such insulin was first prepared so that 1 ml contained 1 unit.

Subsequently the "clinical unit" was adopted. It was one-third the original Toronto unit, and was defined as one-third of the amount of material required to lower the blood sugar of a 2-kg rabbit which has fasted for 24 hours from the normal level of 0.118% to 0.045% in 5 hours. In 1925 a unit based on a definite weight of a sample of crystalline insulin hydrochloride prepared by the National Institute for Medical Research was accepted internationally. Simultaneous determinations of the activity of this sample made by the National Institute, the Insulin Committee of the University of Toronto, and three other laboratories in the U.S.A. and in this country, varied only between 8.4 and 8.8 clinical units per mg. of the dried preparation. It was agreed to regard this sample as containing 8 units. In 1925 the Health Organisation adopted a new reference sample, consisting of a more highly purified sample of insulin preserved in an atmosphere of dry nitrogen at a temperature below 0°, and stored at the National Institute for Medical Research and also at Toronto. This contains 22 units per mg. The unit of the B.P. is the activity contained in such an amount of this standard preparation as the M.R.C. may indicate to be equivalent to the international unit.

**Dose.**—(B.P.) By subcutaneous injection, 5 to 100 units.

Commence with 5 units twice a day—half an hour before breakfast and supper respectively. Most of the food should be taken in these two meals. If after 3 days of this dosage glycosuria still persists, the dose must be raised gradually, first to 10 and 10, and later 15 units or more, if required. On the 7th day test every

2 hours to get a further idea of the effect. By the 11th day all sugar and acetone may have disappeared from the urine, and the blood picture may have become normal. This may represent the permanent balance of diet and insulin, but more often the patient's pancreas improves so that the 13th day 15 and 10 units are too much—12 and 8 units may suffice. Patient's tolerance may continue further, and still less insulin may be needed.

To avoid the violent changes in blood sugar from the 7 a.m. fasting level to the 10 a.m. hyperglycæmia following breakfast and back again to a hypoglycæmic condition between 10 a.m. and lunch, it is now the practice at the Ministry of Pensions Hospital to split the before-breakfast dose into a smaller fraction at 6 a.m. and a larger fraction just before breakfast at 8 a.m. Outside patients should prepare their syringe with the requisite dose overnight, set their alarm clock half an hour before they normally wake up, and give themselves an injection when the clock rouses them, remaining in bed for not less than half-an-hour after the injection. Produces a greater sense of well-being and very marked reduction in the total quantity of insulin necessary.—J. H. Hebb, *Brit. med. J.*, 1/1934, 823.

The most common error is to give too little insulin. Many doctors seem afraid to give doses of more than 10 units twice a day. The proper dose is that which the patient needs, and is always an individual one. Another difficulty is the necessity of varying dosage from time to time. No patient can continue on the same dose of insulin year in and year out, and if the necessary adjustments are not made, the patient will not be kept well. In added illness, especially a febrile one, the whole blood sugar picture moves upwards with the same dose of insulin, and ketosis might result and the patient be liable to go into diabetic coma. Therefore, in any added illness, it is essential to increase the insulin, this is most easily done by adding to the two daily doses a third in the middle of the day. When sickness and vomiting occur, if the patient can keep nothing down, it is a mistake to cut off the insulin entirely, but half the usual dose should be given, otherwise the blood sugar will rise.—R. D. Lawrence, *Brit. med. J.*, 11/1935, 1066.

**Technique of Injection.** Insulin is given subcutaneously (it may be given intravenously in coma), the skin having been previously sterilised. Wherever possible, patients should always be taught to give their own injections, the best sites being the front of the thighs, the abdomen and the lower part of the chest. Before breakfast the abdomen is a good site, and during the day the thigh in women and the skin below the knee in men are the most convenient. Pain is minimised by using a fine sharp needle and inserting at right angles to the skin. To avoid local fatty atrophy the site of injections is changed every week or 10 days, and no two punctures should be made in exactly the same spot within 24 to 48 hours.

The sting due to the acidity of the injection can be entirely prevented by mixing in the syringe one-quarter the volume of 6% sterile sodium bicarbonate. The alkali must not be introduced into the insulin bottle.—R. D. Lawrence, *The Diabetic Life*, 1934.

Atrophy (3 cases) of subcutaneous fat at site of insulin injections, possibly due to presence in insulin of fat-splitting ferment. Site of injections should be varied as much as possible.—E. A. Carmichael and G. Graham, *Lancet*, 1/1928, 601.

Wasting effect on subcutaneous injection.—W. W. Jeudwine, *Brit. med. J.*, 1/1931, 1145.

Local absorption of fat due to insulin injections.—L. R. Woodhouse Price, *Lancet*, 1/1930, 1015.

To prevent too rapid absorption of insulin after injection, Clausen and Lottrup (Denmark) recommend the addition of small amounts of adrenaline. By this method it was found that patients whose blood sugar had varied greatly

with two injections of insulin daily, and who were often at the point of hypoglycæmia, improved greatly when adrenaline 1 : 50,000 was added to the morning injection and 1 : 25,000 to the evening dose. Most of the carbohydrate was given three or four hours after the morning injection and a moderately small amount with the evening meal, an interval of twelve hours between injections being observed. In two of the cases it was found possible to reduce the insulin to one injection daily, giving as little carbohydrate as possible with the evening meal.—*Per Prescriber*, 1935, 373

**Insulin in Castor Oil**, 100 units to each ml. Larger doses can be given without causing hypoglycæmic symptoms. Vegetable oils are very slowly absorbed and may cause reaction.—*Lancet*, 11/1930, 410.

Insulin in oil gives prolonged effect. Castor oil the best suspending agent. The injection must *not* be given intramuscularly but subcutaneously, e.g., under the skin of the abdomen, the injection being given before the patient rises in the morning. It is claimed that the method will lead to a greater number of recoveries.—O. Leyton, *Lancet*, 1/1929, 362, 756.

Good results with insulin in olive oil—H. Chabamier, *per Prescriber*, 1931, 405.

See also Protamine Insulinate, p 581

**Diet** must be strictly controlled, especially as regards carbohydrate content. For severe cases Lawrence advocates a moderate amount of carbohydrate with a moderate dosage of insulin. The carbohydrate may be 80 to 120 g., which allows enough to satisfy most patients. With this moderate carbohydrate diet, less attention need be paid to the protein and fat, and it usually becomes safe to take these as dictated naturally by the appetite. With moderate carbohydrate diets the insulin required varies between 15 and 50 units per day. High carbohydrate diets are sometimes advocated, with increase in dose of insulin.

Advantages of rich carbohydrate diet.—J. A. Nixon, *Brit med J*, 1/1930, 326. See also *Brit med J*, 1/1931, 309.

Relatively high carbohydrate diet in diabetes. Results at General Hospital, Birmingham.—R. Gittins, *Lancet*, 1/1931, 321

Experience has shown that the assumption that increase in carbohydrate necessitates a proportional increase in insulin dosage is entirely false; although generally speaking it is true that 1 unit of insulin is required to metabolise 1 g. of glucose, this only holds good for the first 15 or 20 units, thereafter large amounts of carbohydrates may be added to the diet only with a relatively small increase of insulin. In America as much as 300 to 350 g. of carbohydrates have been included in the diabetic diet with striking results, though this often necessitates dosage of 100 units daily. Special diabetic foods are not only unnecessary but actually objectionable. High carbohydrate diet clears up the arteriosclerosis common in diabetes by reducing the blood pressure.—S. C. Dyke, *Lancet*, 1/1932, 979.

A new method of treatment, the fundamental idea of which is to give glucose covered by the necessary amount of insulin, as opposed to the general practice of insulin covered by glucose, i.e. give the maximum of sugar and the minimum of insulin. Blood-sugar estimations unnecessary. Diet chart given. Steady and automatic recovery of 41 cases at U.C.H.—H. P. Himsworth, *Lancet*, 11/1932, 165.

The high carbohydrate diets necessitate enormous doses of insulin or great reduction in the fat and protein intake. Although it is claimed that such diets are more satisfactory to the patients, they are less agreeable to most patients in this country.—B. D. Lawrence, *The Diabetic Life*, 1934

The present practice in the Diabetes Clinic of the Ministry of Pensions is to disregard entirely the carbohydrate derived from vegetables in Group A, i.e. green vegetables, on which no restriction is placed, and also the carbohydrate moiety of the protein molecule. Patients are, however, given a definite allowance of carbohydrate in the other forms, the allowance being expressed

as Rabinowitch equivalents; this allows the diet to be varied at will, while roughly fixing the total carbohydrate. The amounts of fat are strictly limited, bacon very restricted, only lean meat allowed, and butter and milk strictly weighed out. **Rabinowitch equivalents** are as follows:—Any one of the following may be substituted for one slice of bread = 1 oz.: Two apples; two oranges; two grapefruit; three level dessertspoonfuls of cream of wheat; three level dessertspoonfuls of any one of the following: Wheat, barley, buckwheat, corn, cornmeal; two level dessertspoonfuls of rice; four heaped dessertspoonfuls of oatmeal; two heaped dessertspoonfuls of dried beans; two heaped dessertspoonfuls of dried whole peas; one cupful of toasted cornflakes; one banana; one potato; five soda biscuits; four teaspoonfuls of jam or marmalade; three teaspoonfuls of sugar. Any one of the following may be substituted for one and one-half slices of bread =  $1\frac{1}{2}$  oz.: One shredded wheat; macaroni, eight strips, each being 8 in. long. *N.B.* The cereals must be measured uncooked.

Each patient as he is admitted is placed on a diet containing carbohydrate 133 fat 61, carbohydrate being added according to the patient's requirements in the form of Rabinowitch equivalents. The patients look extremely well on this régime and adhere to their diets with more strictness than was formerly the case. The records certainly prove correct the conclusions of Rabinowitch and other observers that fat can be replaced in the diet by carbohydrate without increasing the insulin requirements. As to the number of doses of insulin, whilst in most cases of moderate severity two doses daily are usually sufficient, in the most severe cases there will be found considerable fluctuations in the blood-sugar level throughout the day if only two doses are given, and an additional small dose is therefore given when the patient wakes at 6 a.m., which inhibits the post-breakfast rise and the noon hypoglycæmia. Except for this early-morning dose, the best time to give insulin is about 20 minutes before a meal. By giving one or two Rabinowitch equivalents of carbohydrate at 11 a.m. in all cases any danger of hypoglycæmia at noon is prevented.—S. Vatcher and M. Douglas, *J. trop. Med. (Hyg.)*, 1935, 278, 289; see also I. M. Rabinowitch, *Diabetes Mellitus*, 1933

**Hypoglycæmia: Effects of Excessive Dose.** There is a rapid fall of blood sugar following the injection, a minimum being reached in 3 to 5 hours, the effect passing off in 5 to 12 hours according to the dose. The normal amount of blood sugar is 0.08 to 0.12% (fasting), or 0.13 to 0.17% after a carbohydrate meal. If the level falls to 0.06 to 0.07% symptoms of hypoglycæmia appear. In untreated diabetics who have become accustomed to a higher level, symptoms of hypoglycæmia may occur at higher levels.

The early symptoms are weakness, shakiness of the limbs, hunger, nervousness and fear. Mental confusion and diplopia may occur, with sweating and palpitation. Later, convulsions and coma may occur. The condition comes on gradually and is never

dangerous if treated within 15 minutes of onset. Glucose or 2 lumps of ordinary sugar should be taken at once with water, and may be repeated in 15 minutes if needed. If coma occurs dextrose should be given intravenously (1 oz. in 20 to 50% solution), or sugar may be given orally, by stomach tube or *per rectum*.

Hypoglycæmia is dangerous in patients with cardiac complications. Edema may be considerably increased, an attack of angina pectoris brought on, or a paroxysm of auricular fibrillation—*Per Prescriber*, 1929, 409

1 ml. of 1 in 1000 adrenaline solution or 10 units of pituitary extract intramuscularly generally restores consciousness in 5 to 10 minutes. Patients should always carry sugar in pocket and a notice asking that adrenaline and sugar be given if found unconscious—*J. Amer. med. Ass.*, 1/1929, 2168

**Suitability of the Case.** All cases except those suffering from severe acidosis and coma should be given a basal maintenance diet but not put to bed unless severe weakness is present.

The diet must be restricted as to carbohydrates, with a moderate amount of protein and fat. If after a fortnight the patient is not sugar-free, a weighed diet must be given, equivalent to 25 calories per kg. If still not sugar-free, insulin is necessary.

If the urine becomes sugar-free on this, it should be gradually raised to an adequate diet for his ordinary duties. If he remains aglycosuric the treatment with insulin is not indicated. 75% of diabetics can be controlled by diet. If at the end of the week's treatment on basal diet, the urine is not free of sugar, the patient requires insulin.

There is no evidence as yet that the treatment is curative. It is not recommended unless the treatment can be continued. The initial stages of treatment should be carried out in connection with facilities for blood and urine sugar estimations.

No true case of diabetes, however severe, proves refractory to insulin. Failure is sometimes due to renal glycosuria without hyperglycæmia. Hepatic glycosuria is refractory but is not true diabetes. Diabetic cases with cirrhosis of liver take longer but ultimately respond. Some cases of glycosuria may be refractory owing to disorders of thyroid, pituitary or suprarenal. Diabetes complicated by severe infections ultimately responds to insulin, if given big enough doses. Many cases of failure of insulin are due to the patient surreptitiously increasing the diet.—Prof. Marcel Labbé, *per Brit. med. J.*, 1/1927, 530.

Two different types of disease can be distinguished as causing the symptom-complex of diabetes mellitus. One, the insulin-sensitive type, appears to be caused by deficiency of insulin; the other, the insulin-insensitive type, is apparently due not to lack of insulin, but to lack of an unknown factor which sensitises the body to insulin. A test for distinguishing these two types of diabetes mellitus is described. The appropriate dietetic treatment of the two diseases may differ.—H. P. Himsworth, *Lancet*, i/1936, 130.

**Contraindication.** There are no contraindications to the use of insulin, but special care is necessary in angina pectoris, since an excessive dose may precipitate an attack.

Glucose intolerance in various dermatoses. Abnormalities in blood-sugar content—*Lancet*, ii/1929, 1141.

Anaphylaxis due to insulin.—*Brit. med. J. Epit.*, ii/1925, 13.

**Treatment of Coma.** Treat as for collapse, clear bowels with enema, or wash out the stomach and give as much fluid as possible orally, *per rectum*, or preferably intravenously if the patient

cannot swallow If not completely comatose, 2 drachm doses of sodium bicarbonate should be given 2-hourly to counteract acidosis, until the urine becomes alkaline. Give also insulin 40 units with dextrose 40 g. *per os*, repeating every 4 hours until the ketonuria disappears, reducing the insulin if the urinary sugar is decreased in amount. If coma is complete, large quantities of injection of sodium chloride and acacia should be given intravenously, together with insulin and dextrose in quantities as above, the initial dose of each being given intravenously.

Desperate cases treated by 100 units and large volume of gum saline intravenously.—R D. Lawrence, *Brit med J*, i/1930, 690

Diabetic coma usually due to carelessness on part of patient Loss of an hour inexcusable delay Most cases saved by initial dose of 60 units. Fear of hypoglycemia groundless. Early treatment and sufficient dosage essential; a minimum of 200 units necessary to cure coma, with goodly portion of this as initial dose.—W. R. Campbell, *Med. Annu*, 1931, 142.

Three cases with blood sugars above 1000 mg successfully treated by massive doses of insulin (in one case 180 units intravenously during 8 hours), gastric lavage with 2% sodium bicarbonate, and 1500 ml. of 5% sodium bicarbonate and 1500 ml physiological salt solution by hypodermoclysis.—C J. Haines and R. Davis, *J Amer. med Ass*, ii/1932, 24

As a result of a study of 86 patients with diabetic acidosis, the following treatment is recommended.—(1) Immediate parenteral administration (one half intravenously, the remainder subcutaneously and intraperitoneally) of 60 ml of a sixth-molar solution of racemic sodium lactate per kg. of body weight (2) Immediate administration of 2 units of insulin per kg. of body weight (3) Administration of 40 ml of Ringer's solution per kg. of body weight as soon after the administration of sodium lactate as possible (4) Repeated administration of insulin 6 hours later in a dose of 0.5 unit per kg. of body weight. (5) Transfusion of citrated whole blood or plasma (20 ml. per kg. of body weight) if oedema due to reduced plasma protein develops.—A. F. Hartmann and M. Morton, *Arch. intern Med*, 1935, 413

#### Rules for Distinguishing Insulin Coma from Diabetic Coma:

IN INSULIN COMA —(1) Skin usually very white, but may be normal in colour. (2) Breath does not smell of acetone (3) Respiration shallow. (4) Eyeball tension normal or raised. (5) Urine usually sugar-free, but may contain sugar if bladder has not been emptied for some hours (6) Urine need not contain acetoacetic acid to Rothera's test, but may do so if bladder has not been emptied for some hours (7) Blood sugar below 70 mg. per 100 ml and may be as low as 40 mg. per 100 ml IN DIABETIC COMA —(1) Skin usually flushed. (2) Breath smells of acetone. (3) Respirations deep. (4) Eyeball tension much lower than usual (5) Urine always contains large amounts of sugar (6) Urine always contains large amounts of acetoacetic acid (7) Blood sugar is over 200 mg per 100 ml, and may be up to 500 to 800 mg per 100 ml —G. Graham, *Med Pr.*, 1934 (Symposium No. 1).

Testing Expired Air for Acetone. Moisten a watch-glass with Scott-Wilson reagent and hold close to patient's mouth and nose for 2 or more minutes Acetone reaction shown by clouding of the reagent Of practical value in the differential diagnosis of the unconscious state, e.g., diabetic coma —A. Wallhauser, *J Amer. med. Ass.*, ii/1928, 21.

### GENERAL REFERENCES

(For references to earlier work on diabetes see previous editions)

ACETONURIC VOMITING of children from 4 to 6 years well treated with 10 to 15 units of insulin subcutaneously, followed by carbohydrate meal. Effect of insulin lasted three hours.—Per J. *Amer. med. Ass.*, ii/1925, 1167.

ASTHMA. Five units of insulin twice daily, gradually increased to 10 or 12 units, with an ounce of glucose an hour after each dose, for 3 weeks together with ultra-violet rays and agar-serum peptone, of value.—A. G. Auld, *Brit med. J.*, i/1929, 992.

DIABETES Only one diabetic patient seen who failed entirely to respond to insulin administration —Prof H. Maclean, *The Results of Insulin Therapy in*



Diabetes Mellitus, *B.M.A.*, 1927; *Brit. med. J.*, ii/1927, 1015. See also *ibid.*, Prof. K. A. Petren, 1019 and P. J. Cammidge, 1020.

Personal experiences with insulin. Previously forced to give up work and live on starvation diet. Now able to do 14 hours work a day.—R. D. Lawrence, *Brit. med. J.*, i/1931, 1077.

In 1922 the average life of a diabetic was 6 years, to-day patients who started treatment with insulin on its introduction 9 years ago are still alive, and a growing percentage outlive their life expectancy.—E. P. Joslin, *J. Amer. med. Ass.*, ii/1931, 595.

The question, "Does insulin cure diabetes?" can be answered by "Yes, if given in adequate doses and the patient can be protected from adverse influences." The ideal is to arrange food and doses of insulin to keep the sugar content of the blood between 0.08% and 0.15% during the 24 hours. In severe cases on a diet fairly rich in carbohydrate this may mean 3 or even 4 injections in the 24 hours for a time, but it is a great exception for more than two to be needed for longer than 6 months. "Adverse influences" include the taking of alcohol and the action of toxins.—O. Leyton, *Lancet*, ii/1933, 120.

The answer to the question "Will insulin cure me?" is that insulin cures diabetes as food cures hunger. Hunger recurs after a few hours, and the need for insulin also recurs. A wooden leg enables a lame man to walk, but not to grow a new leg. When the artificial leg is removed he falls to the ground. But the disease can certainly be arrested and health restored by insulin. It is wrong and untrue to offer more.—R. D. Lawrence, *The Diabetic Life* (1934).

Prognosis of diabetes in children. "Before the discovery of insulin the mortality of diabetes in childhood was nearly 100%, and to-day diabetes as a cause of death in the young has disappeared nearly to the vanishing point." (Priscilla White, *Diabetes in Childhood*). No gloomy prognosis is justified in this insulin era, but continuous care and treatment are certainly necessary, and in practically every case insulin injections. Children should be placed on an adequate diet, liberal in carbohydrate and total calories, and the correct amount of insulin carefully worked out to metabolise it. A cure is not possible, but growth and development proceed normally and average weight is maintained.—R. D. Lawrence, *Lancet* i/1934, 807. See also L. Cole, *ibid.*, 947, 998.

Whereas in 1931 the number of prescriptions issued by insurance practitioners was 155,000, representing the disbursement of about 57 million units, in 1932 the number of prescriptions rose to 181,987, in 1933 to 201,252, and in 1934 to 288,541. It is estimated that, to insured persons alone, about 111 million units were issued in 1934, or not far short of double the number of units issued in 1931.—*Rep. med. Offr. Minist. Hlth, Lond.*, 1934, 158.

DIABETES MELLITUS AND HEREDITY. The marriage of diabetics is clearly inadvisable, and intermarriage between families where there is even a remote history of the disease is to be discouraged, and where such marriages occur the children and grand-children, even to the third and fourth generation, should be watched and guarded as far as possible from exciting causes likely to develop a latent and inherited defect.—P. J. Cammidge, *Brit. med. J.*, ii/1928, 741. See also Joseph A. Parkes, *ibid.*, ii/1929, 1008.

DYSMENORRŒA. In a group of twelve patients, all nulliparas, suffering from primary or essential dysmenorrhœa, ten received practically total relief from menstrual pain by using insulin (from 7 to 10 units daily) from 3 to 7 days before or during the period. One patient obtained relief in one period with one type of insulin and no relief during another period with another type of insulin. Another patient was only partially relieved.—A. Altschul, *J. Amer. med. Ass.*, i/1936, 1383.

EXOPHTHALMIC GOITRE well treated by insulin, 5 to 30 units twice daily.—E. G. B. Calvert, *Brit. med. J.*, ii/1924, 835. See also *J. Amer. med. Ass.*, ii/1925, 1522, and *ibid.*, 1007. Improvement in 2 out of 4 cases with injections of 60 to 100 units daily.—R. D. Lawrence, *Brit. med. J.*, ii/1924, 753, *Brit. med. J. Ept.*, ii/1924, 13.

Of value only in the pancreatogenous type of exophthalmic goitre, but fails in cases of thyroid origin, and those due to primary hypophyseal disease.—O. Klein, per *Brit. med. J. Ept.*, i/1926, 56.

Insulin in treatment.—*J. Amer. med. Ass.*, ii/1925, 1098. Action variable and inconstant.—M. R. Castex, per *Prescriber*, 1926, 214.

HEART DISEASE. Of value in congestive heart failure, especially in arterial and coronary syndromes. Six cases of intractable angina pectoris successfully treated with 5 units of insulin before breakfast and before the evening meal,

each dose followed by 30 g. of dextrose taken with the meal, the patients continuing to take any remedies they had previously been taking. Treatment continued for from 2 to 17 weeks. It is believed that anginal pain is related to faulty carbohydrate metabolism in the heart, and that insulin acts by its stimulating effect on glycogen metabolism in the heart and progressively by promotion of the combustion of fat, the process leading to resolution of early atheromatous changes in the coronary arteries—K Shirley Smith, *Brit med J*, 1/1933, 696.

**MENORRHAGIA AND METRORRHAGIA.** Moderate doses injected twice daily before morning and evening meals of value—usually effective within 2 or 3 days. The action of insulin is not specific, but is related to that of the ductless glands other than the pancreas—*Brit med J Ept*, 1/1928, 13.

**PREGNANCY, VOMITING OF.** Combined use of dextrose intravenously with insulin hypodermically—about 2 g dextrose in 10% solution to each unit of insulin—of value in excessive vomiting of pregnancy and in eclampsia.—*J Amer med Ass*, 1/1926, 557.

**PULMONARY TUBERCULOSIS.** Increased appetite and progressive increase in weight with subcutaneous injections of 5 units before meals—Morin and Bouessée (Leyzin), per *Prescriber*, May 1928, 187.

**SCHIZOPHRENIA.** Treated by hypoglycæmic shock, produced by means of huge doses of insulin. Method is dangerous, but 70% of full remissions claimed, although these were all early cases—*Lancet*, 1/1936, 1018.

**SKIN DISEASES.** Insulin in treatment—M Ferond, per *Prescriber*, 1926, 344.

**TONIC ACTION.** Of value for increasing the weight of persistently thin people, the dose being 10 units 3 times a day about 20 to 30 minutes before meal, accompanied by a liberal, unmeasured diet. Treatment continued for several weeks. Patients gained weight rapidly and immediately, the increase tending to become less marked as weight approached normal standard, and the weight remaining constant, or continuing to increase, on omission of insulin. Local skin hypersensitiveness occurs in some cases, but hypoglycæmic reactions rare. Insulin serves as an admirable tonic both physiologically or psychologically—H. Blotner, *J. Amer med Ass*, 1/1933, 91.

**VARICOSE ULCERS.** Insulin injected, and locally, found of value—*Pharm J*, 11/1925, 180. Ulcers of leg well treated—*Brit med J Ept*, 11/1925, 10.

Insulin applied locally (12 units twice a day in the form of a wet dressing) completely healed a resistant non-diabetic ulcer of 5 months' standing in 10 days—Per *J Amer med Ass*, 11/1925, 473.

### Insulin Products for Oral Use in Diabetes.

In view of the obvious disadvantages of the administration of insulin by injection, numerous attempts have been made to produce compounds which would withstand the action of the digestive enzymes and thus be active when given orally. Although success has been claimed for a variety of compounds, none of these claims has so far been substantiated. Among the preparations put forward are compounds or mixtures of insulin with saponin, bile acids and blood-serum.

**Inunction of Insulin.** Inunction in 6 children. It was proved that insulin is easily absorbed by the intact skin, its action being greater in infants than in children of more advanced years. In the case of an infant of 1 year, weighing 9 kilos, insulin inunction reduced concentration of sugar in blood so successfully that experiment had to be discontinued prematurely—*Lancet*, 1/1924, 407.

Insulin used as an inunction in almond oil, in hydrous wool fat, and in alcohol and glycerol, was found to have no therapeutic value—*Quart J Med*, 1927, 187.

[P187] **Protamine Insulinate.** A preparation developed by Hagedorn consisting of a compound of insulin hydrochloride with a protamine obtained from the sperm of a species of trout, *Salmo iridius*. The preparation is absorbed more slowly than insulin hydrochloride itself, so that the action of the insulin is spread

over a longer period and the effect on the blood sugar is more even and more prolonged.

Protamine insulinate is injected as a colloidal suspension. The suspension is not stable for more than a few weeks, and it is therefore produced freshly by adding an alkaline buffer solution to the protamine insulinate solution (which is stable for at least  $1\frac{1}{2}$  years) so as to adjust the pH to the isoelectric point, pH 7.3.

The sharp peak effect usually seen 3 or 4 hours after the injection of ordinary insulin is largely avoided by the use of protamine insulinate. Furthermore, the effect is more prolonged—roughly about twice as long as that of ordinary insulin. Without increasing the number of injections one can, by this means, diminish the blood sugar fluctuations, reduce or suppress the glycosuria and reduce the ammonia excretion, and at the same time reduce the risk of the occurrence of hypoglycæmia. No ill effects have been observed. The injection is painless, there is no local reaction, protein reactions do not occur, and failure of the insulin effect has never been observed. The effect seems to be the same whether the patients stay in bed or are out of bed. It has been as effective in children as in grown-up persons. The administration as a suspension has never given rise to difficulties or inconvenience. In acute conditions (coma), ordinary insulin is, of course, to be used, as it works faster. When the treatment with ordinary insulin gives satisfactory results, the use of protamine insulinate is of no special value. The best results have usually been obtained by giving the patients ordinary insulin in the morning and protamine insulinate in the evening, but there are some cases in which the result will be the best with protamine insulinate both morning and evening. Then it usually pays to give the injections at equal intervals, say at 8 a.m. and 8 p.m.—H. C. Hagedorn *et al.*, *J. Amer. med. Ass.*, i/1936, 179.

Clinical trials on two young, severe diabetics who showed rapid oscillations of blood sugar after ordinary insulin, demonstrated that protamine insulinate acts more slowly and for a much longer period than ordinary insulin, and a large dose can act for more than two days. It is much weaker in dealing with carbohydrate food, and usually cannot prevent hyperglycæmia after meals. In contrast, its action on endogenous sugar is nearly as rapid and good as ordinary insulin. It causes less symptoms of hypoglycæmia than ordinary insulin, even at the same blood-sugar concentration. Protamine insulinate is certainly absorbed more slowly from the subcutaneous tissues. It therefore has qualities which promise great use in severe diabetics with oscillating blood sugars and rapidly recurrent ketosis. On the other hand, it is not strong enough in its action to control ingested carbohydrate, so that the use of ordinary insulin before carbohydrate meals and protamine insulinate in the evening has been advocated and is necessary to obtain full control of the diabetic condition—R. D. Lawrence and N. Archer, *Brit. med. J.*, i/1936, 747.

Clinical observations on 20 patients indicate that the immediate effect of insulin-P (insulin protamine compound) is much less than that of insulin-R (regular insulin). When the former is used alone, and given as a single dose before breakfast, the meals of the first few days provoke glycosuria, but when the dose is properly adjusted the level of the blood sugar on successive mornings decreases progressively and the elevating effect of meals diminishes until, by the end from of 4 to 6 days, a normal level of blood sugar may be attained, even in cases of severest diabetes. Supplementing insulin-P with small doses of insulin-R will shorten the period of obtaining control. Insulin-R should not be mixed in the same syringe or injected into the same site with insulin-P. It has not been necessary to continue the supplementary use of insulin-R after the first few days in the milder cases, but probably in many cases such supplementary use of insulin-R will be desirable, especially in emergencies. Until more experience has been obtained it would appear that insulin-R will be the insulin of choice when quick action is desirable, as in the treatment of acidosis. Although insulin-P, in many cases, makes possible effective management of diabetes with only one administration of insulin a day, and with less insistence on rigid control of the diet, its careless use or disregard of the diet is attended with danger.—R. G. Sprague and co-workers, *J. Amer. med. Ass.*, i/1936, 1701. [P1 87] **Leo Insulin Retard** (Nordisk Insulinlaboratorium, Copenhagen; Bencard, London). A preparation of protamine insulinate issued in 5 ml. ampoules of a solution containing 40 units per ml, together with a 1% solution

of sodium phosphate. In use 1 ml. of the sodium phosphate is added to a 5 ml ampoule, the mixture thoroughly shaken and the requisite dose injected. The mixture must be vigorously shaken each time before use. The unmixed solutions are stable for 1½ years, but if mixed the resulting suspension is stable for not more than a few weeks. The dilution of the insulin by the buffer solution can generally be ignored in calculating dosage.

**Protamine-Zinc-Insulin.** A protamine insulinate compound containing zinc stated to have more prolonged action, and at the same time to be effective in diabetic acidosis.—I. Rabinowitch, *Canad. med. Ass. J.*, 11/1936, 239. See also *Brit. med. J.*, 11/1936, 724.

The addition of a small amount of zinc chloride to insulin (e.g., 1 mg of Zn to 500 units) before adding the protamine greatly prolongs the hypoglycæmic action. Equally effective protamines are obtainable from the testes of the coho, steelhead and spring salmon and from the rainbow trout—D A Scott and A M Fisher, *J. Pharmacol.*, 1936, 58, 78.

### OTHER PREPARATIONS FOR ORAL USE IN DIABETES.

**Galega.** Doses of 80 to 100 drops twice daily by mouth of a liquid extract of galega, standardised to contain 3% of the alkaloid, galegine, of value in diabetes. Its action resembles that of Synthalin (*vide postea*), and it is quite harmless and without contraindications. It is active both in mild and in moderately severe diabetes, and is especially useful in insulin-resistant cases.—G. Parturier and G. Hougonot, *Pr. méd.*, 1935, 258.

**Galegin**, the alkaloid of *Galega officinalis*, has a similar constitution to Synthalin, and has been used for reducing blood sugar, replacing 20 to 30 insulin units. No secondary effects observed—*Pharm. J.*, 11/1927, 563.

**Glucosone**, or aldofructose (one of the oxidation products of dextrose or fructose) has similar properties to insulin and is given by the mouth—P T. Herring, *Lancet*, 1/1927, 1000.

[P1-81] **Synthalin** and [P1-81] **Synthalin-B** (Schering, London). Decamethylene diguanidine dihydrochloride and the corresponding dodecamethylene compound respectively in tablet form. They reduce glycosuria and the blood sugar when given orally. Synthalin-B is milder in action but is better tolerated. Have been recommended for slight cases or for use in conjunction with insulin. Synthalin tablets contain 0.01 g and may be given twice a day with an interval every fourth day. Larger doses may be given if tolerated.

Synthalin-B tablets contain 0.005 g. Treatment may commence with 1 tablet 3 times on the first day followed by 2 tablets thrice daily subsequently, with an interval every fourth day.

Treatment in all cases should commence with rendering the patients sugar-free by diet, then giving carbohydrate so that excretion of sugar in urine is 25 to 40 g per day.

Preliminary reports to the Medical Research Council show Synthalin to be unsatisfactory—*Lancet*, 11/1927, 517, *ibid.*, 649. Results uneven—G. Graham and R D Lawrence, *Brit. med. J.*, 11/1927, 1143.

In rabbits, Synthalin or decamethylene-diguanidine, in large doses was toxic. The fate of the glucose was not quite clear.—H H. Dale, *Brit. med. J.*, 11/1927, 1141.

The name Synthalin was applied to the methyl ester of piperonyl-quinoline carbonic acid. Danger of identity of name for two totally different substances.—*Yearb. Pharm.*, 1927, 298.

Unsatisfactory, if not dangerous, for use in diabetes in man—Prof J. R. MacLeod, *Brit. med. J.*, 1/1930, 919, *Lancet*, 11/1930, 518.

Reduction of blood sugar after oral use due to injury of parenchyma of liver and not to increased capacity of body to burn sugar—*Lancet*, 11/1931, 412.

Since 1927, Synthalin has been continuously used in the Bristol Royal Infirmary, and 70% of diabetics are now treated with it in place of insulin. Given correctly, it is devoid of danger and gives results equal to insulin. Carbohydrate is allowed fairly liberally, the relation of fat to carbohydrate in grammes in the four stock diets being: F/C=107:180, 137:186, 165:220, 170:238. Commence with 2 tablets (10 mg) beta-Synthalin morning and evening after meals, with 1 tablet of dehydrocholic acid to every 2 of Synthalin. Increase dosage in these proportions to limit of tolerance or until diminution of glycosuria occurs and then reduce to necessary minimum, with rest every third day. A phosphate mixture is taken thrice daily. Liver replaces meat one day, and

sweetbreads half the meat of another day, with Bemax or Marmite daily  
A. T. Todd and co-workers, *Practitioner*, 1/1932, 531

[P1 81] **Anticomman** (*Riddell, London*). Decamethylene-diguanide bitartrate, pancreas ferment (lipase), sodium phosphate. Tablets for the oral treatment of diabetes in severe cases as adjuvant to insulin injections.

*For a full account of the chemistry and physiology of insulin with several hundred references to original papers see "Insulin, its Production, Purification and Physiological Action," by D Hill and F. Howitt (1936). For the treatment of diabetes, see "The Diabetic Life," by R D Lawrence (1934)*

## IODOFORMUM

B P, U.S.P. XI, P. *Helv* V, P *Dan*.

$\text{CHI}_3 = 393.8$ .

*Syn.* TRI-iodomethane.

*Dose.*— $\frac{1}{2}$  to 3 grains (0.03 to 0.2 g.).

Yellow crystals or unctuous powder with characteristic odour. Contains 96.7% of I. M.p.  $120^\circ$  to  $122^\circ$ .

To cover its odour it may be mixed with coumarin, 1 in 50, or with menthol, phenol, thymol, oils of anise, eucalyptus, geranium, peppermint, rosemary or sassafras, about 1 or 2%.

To remove the smell from the hands, utensils, etc., rub with a little crushed linseed and wash afterwards.

**Manufacture.** By acting upon alcohol with iodine in the presence of caustic potash (or carbonate) solution at about  $70^\circ$ , or by the electrolysis of an aqueous solution of potassium carbonate, potassium iodide and alcohol

**Soluble** 1 in 8 of ether, 1 in 10 of ether (sp. gr 0.735), 1 in 10 of chloroform, 1 in 100 of 90% alcohol, 1 in 14 of eucalyptus oil, 1 in 10 of collodion, 1 in 60 of soft paraffin and oil of almonds, and about 1 in 30 of olive oil. Almost insoluble in water, but soluble 1 in 10 of Rubini's solution of camphor, which disguises its odour

**Incompatible** with calomel, silver and other nitrates, potassium chlorate, nitrites and methylated spirit.

**Antidotes.** Give sodium bicarbonate freely, in plenty of water. Keep patient warm and give brandy,  $\frac{1}{2}$  oz, or aromatic spirit of ammonia,  $\frac{1}{2}$  dr, in water. Bromides, in 60 gr. doses, if necessary.

Given internally it may bring out a rash.

**Uses.** Antiseptic, anæsthetic and sedative. Useful in gonorrhœa and syphilis (non-irritant). For sores as dusting powder or in ethereal solution. Insufflations are used in throat affections The ointment is a useful dressing for wounds.

Taken internally, iodoform decomposes and iodine is soon found in the urine. It has given good results in intestinal hæmorrhage, tertiary syphilis and cirrhosis of the liver, also to kill tape-worm. Tuberculous peritonitis has rapidly recovered under mercury and chalk  $\frac{1}{2}$  gr. with iodoform  $\frac{1}{2}$  gr. thrice daily. Oral administration

has also been found useful in pulmonary and other forms of tuberculosis. Excessive administration may produce symptoms like those of exophthalmic goitre in susceptible persons.

**AMOEBIASIS** Nine cases of subacute and chronic amœbic colitis satisfactorily treated. Patient kept in bed on a fluid or very light diet, and after a preliminary purge (magnesium sulphate 15 g.), iodoform is given in the form of keratinised capsules containing 0.05 g., 1 or 2 capsules 3 or 4 times a day for 12 to 15 days. The treatment may be repeated after an interval of 1 week. Toxic symptoms not noted except in one patient who complained of vertigo. No rash noted. —Sir A. Castellani, *J. trop. Med. (Hyg.)*, 1935, 268.

**LEPROUS ULCERS** well treated by application of 16 gr. to 1 oz. of acetone for small ulcers and 10% iodoform in eucalyptus oil for large and sloughing ones —M. C. Lang, per *Med. Annu.*, 1931, 278.

**PLEURITIC EFFUSION.** Iodoform intrapleurally, as an emulsion in glycerin, olive oil and ether (1 in 9), in 1 or 2 doses of 1 to 2 ml., gave good results —Per *Practitioner*, 1/1928, 264.

**Carbasus Iodoformi (B.P.C.).** IODOFORM GAUZE 5%.

**Cereoli Iodoformi et Eucalypti.** *Syn.* IODOFORM AND EUCALYPTUS BOUGIES. Iodoform 5 gr., eucalyptus oil 10 m., oil of theobroma 35 gr. To make a bougie 4 inches long. Used for acute gonorrhœa. When the symptoms have subsided, any remaining discharge may be treated by zinc sulphate injections.

**Collodium cum Iodoformo.**

Iodoform 1, collodion 12. *P. Jap.* and *Fr. Cx.* have 1 in 10.

Acetone collodion will dissolve 5%. A pigment for venereal sores.

**Glycerinum Iodoformi (B.P.C.).** *Syn.* EMULSIO IODOFORMI.

Iodoform, in fine powder, 1, alcohol 90% *q.s.* to moisten, glycerin 7, sterilised water 2. Mix well in above order.

*St. B. H.* and *G. H.* are the same. *K. C. H.* has iodoform (washed with 1 in 20 phenol solution) 1 part, glycerin 9 parts.

For injection, well diluted, into the bladder and into sinuses. Most effective before caseation has occurred. For filling a cavity in the bone, after removing caseating tissue, iodoform 1 and boric acid 4 is useful.

**Guttæ Iodoformi Compositæ (Brompton H.).** (For the ear)

Iodoform 5 gr., ethyl acetate 2 dr., alcohol 90% 2 dr., glycerin to 1½ oz.

**Injectio Iodoformi.** (For bladder injection.)

Iodoform in fine powder 1, mucilage of tragacanth 2, water 7. This is less irritating than the glycerin emulsion (should be diluted 20 to 40 times with warm water).

**Insufflatio Iodoformi.**

Iodoform 2, starch (carefully dried) 1. In specific affections of the throat, antiseptic and mildly caustic.

[D P1 81] **Insufflatio Iodoformi Composita.**

Iodoform 6, boric acid 6, morphine acetate 1.

**Oculentum Iodoformi (B.P.).** 4% in Oculentum Simplex.

**Oleum Iodoformi et Creosoti.** *Syn.* HUILE CREOSOTÉE IODOFORMÉE.

Heat olive oil 70 to 120° for 10 minutes. When cold add creosote 5, guaiacol 1, and iodoform 10, lastly ether 30.

**Iodoform Oil** (20 gr. to 1 oz. of olive oil) is useful as a dressing in the early stages of recovery after operation for fistula, the oil facilitating packing with dressing. The first few dressings in these cases are usually painful.

[P2 81] **Pasta Iodoformi (R.D.H.).**

Iodoform 6, tannic acid 1, liquefied phenol *q.s.* to make a paste.

**Cinnamon Paste (Iodoform Paste)** is used by dentists and understood to mean iodoform mixed into a paste with cinnamon oil. Used for treating septic root canals.

**Pencils of Iodoform**, the thickness of a No. 9 catheter, for uterine medication, are prepared with iodoform 15%.

**Pigmentum Iodoformi Compositum** (*B.P.C.*). *Syn.* IODOFORM VARNISH, WHITEHEAD'S VARNISH.

10% *w/v* with benzoin, storax and balsam of tolu in ether. For surgical use.

**Pigmentum Iodoformi** (*Gt. Orm. H.*). WHITEHEAD'S VARNISH MODIFIED.

Iodoform 1 dr., benzoin varnish 10 dr. (Benzoin varnish is Benzoin 4 dr., colophony 3 dr., balsam of tolu 1 dr., ether (0.720) 5 oz.).

Cheap and effective: does not retract the skin, dries well, and remains elastic. Clean, antiseptic, and mildly stimulating.—J. W. Peck, *Brit. med. J.*, ii/1931, 681.

**Pulvis Iodoformi et Acidi Borici** (*B.P.C.*). Iodoform 1, boric acid 3.

**Suppositorium Iodoformi** (*B.P.*) contains 3 gr. of iodoform in oil of theobroma. 1 gr. and 5 gr. suppositories are also made. For fissure of the anus and irritating hæmorrhoids.

**Unguentum Iodoformi** (*B.P.C.*). 10% in simple ointment *R.L.O.H.* has 60 gr. in yellow soft paraffin to 1 oz.

**Unguentum Iodoformi et Eucalypti** (*B.P.C.*). Iodoform 2% and oil of eucalyptus 20% in a paraffin basis.

**Mencièr's Solution "A."** For embalmment of wounds. Iodoform 10, Peruvian balsam 30, guaiacol 10, eucalyptol 10, ether 100.

**Solution "B"** is the same with ether to 1000.

**Formidin.**

*Dose.*—1 to 5 grains (0.06 to 0.3 g.).

Stated to be a compound of salicylic acid, formaldehyde and iodine,  $C_{11}H_{11}O_4I_2$ , containing approx 50% of I.

A white powder insoluble in water, alcohol and dilute acids.

It decomposes in the presence of alkali, hence used as intestinal antiseptic. Applied locally in skin affections. Its action is said to be due to the splitting off of salicylic acid, formalin and iodine.

**Iodopyrrolum.** *Syn.* IODOL, TETRA-iodo-PYRROL.  $C_4HNI_4 = 570.7$ .

*Dose.*—1 to 4 grains (0.06 to 0.25 g.).

Nearly odourless brownish powder containing 89% of I, obtained by acting on pyrrol with iodine in presence of alcohol. It explodes if rubbed with mercuric oxide. Decomposes at 140°.

**Soluble** 1 in 155 of glycerin, 1 in 6 of absolute alcohol, 1 in 18 of alcohol 90%, 2 in 3 of ether, 1 in 150 of chloroform, also in oils. Insoluble in water.

**Uses.** Painless wound dressing for buboes, ulcers, and ear discharges.

An ointment 1 to 5 of soft paraffin, and a solution 3 parts to 35 of alcohol and 62 of glycerin have been used for granular and chronic conjunctivitis with good results. A solution of iodol 1, alcohol 3, glycerin 21 may be used as a pigment in diphtheria, also iodol 2, menthol 1, almond oil 96, for throat spray or pigment.

1% of menthol covers the odour of iodol and is said to render it more active.

## IODUM

*B.P., U.S.P. XI, P. Helv. V, P. Dan.*

$I = 126.9$

*Dose.*—*U.S.P.* average dose  $\frac{1}{8}$  grain

In heavy, bluish-black crystals or plates. Is obtained from kelp or from the mother liquors of Chili saltpetre.

The following medicinal inorganic iodides contain the halogen approximately in these proportions.—Ammonium iodide 87.5%, lithium iodide, 94.75%, potassium iodide 76.4%, rubidium iodide 59.75%, sodium iodide 84.6%, strontium iodide ( $\text{SrI}_2 \cdot 6\text{H}_2\text{O}$ ) 56.45%.

**Soluble.** About 1 in 5000 of water, 1 in 12 of alcohol 90%, 1 in 4 of ether, 1 in 30 of chloroform, 1 in 65 of glycerin, 1 in 6 of carbon disulphide. Very soluble in concentrated solutions of potassium iodide.

**Incompatible** with alkalis, alkaloids, starch, soluble lead and mercury salts, phenol, chloral hydrate and sodium thiosulphate.

**Antidotes.** Give copious draughts of mucilage of starch, or flour, etc., and water; or 20 to 30 gr. of sodium thiosulphate in water. Then empty stomach by emetic or by stomach tube, using thin starch or dilute sodium thiosulphate solution. Keep the patient warm; give demulcent drinks freely. Strychnine,  $\frac{1}{8}$  gr., hypodermically. Morphine,  $\frac{1}{4}$  gr. hypodermically, if pain is severe.

**IODIDE ERUPTION**, a case of granulomatous form which is rare. Treatment was sodium chloride 10 to 20 gr. three times daily after meals. Said to have been attended with dramatic effect in cases of bromide eruption. Slow recovery.—H. C. Semon, *Lancet*, 11/1926, 803

**Uses.** Internally is variously used as tincture *q.v.* in influenza, catarrhs, epilepsy, and to reduce obesity.

Externally iodine is a powerful germicide, but it irritates the skin and will blister if too strong. As a counter-irritant the weak solution is painted on chilblains, over inflamed joints, spots of pleurisy, sore gums and scrofulous glands, to abort boils, and is injected as weak solution to cure hydrocele, *cf.* also Morton's Fluid for spina bifida. It is a useful application for ringworm (*cf.* Coster's Paste) and is inhaled to check profuse expectoration in chronic bronchitis. In puerperal sepsis as a douche—*vide* Injectio Iodi

A mouth-wash of 30 m of the weak solution to 1 oz. of water is useful in mercurial stomatitis. Painting the face with the weak solution, diluted if painful, has been advocated for the prevention of pitting in small-pox and chicken-pox, but is usually ineffective. Catgut (*q.v.*) is sterilised by immersion in 1% alcoholic solution

#### REFERENCES TO IODINE THERAPY

**ACTINOMYCOSIS.** Tincture of iodine in milk. *Dose*.—5 to 10 minims in half a cup of water three times a day. "Effect almost incredible."—H. Chitty, *Brit. med. J.*, i/1926, 419; i/1929, 347. See also *Prescriber*, 1929, 345.

**BERI-BERI** well treated with tincture of iodine, 5 drops in a tumbler of water daily.—H. W. Ridley, *J. trop. Med. (Hyg.)*, 1925, 103.

**COLDS.** Iodine 8 or 10 drops of 1% solution, twice daily, fasting, is specific.—*Per Prescriber*, Jan. 1923, 14.

**CORNEAL ULCERS** treated by a 1:20 or 1:30 tincture of iodine after preliminary use of cocaine. The iodine is taken up on a probe or glass rod and held in the air a minute or two for the alcohol to evaporate, then the ulcer touched with it. The iodine is therefore almost solid and cannot diffuse.—*Prescriber*, 1920, 310, 311. See also Eye affections, under Intravenous Iodine *postea*.

**DIARRHŒA.** Tincture of iodine, 5 drops twice daily for adults and 2 drops twice daily for children, of value in acute diarrhœa or chronic colitis, and in apparent bacillary dysentery, pending bacteriological report. Must not be used in connection with other anti-dysenteric or anti-diarrhœic medication.—F. C. de Mendoca, *J. Amer. med. Ass.*, ii/1929, 1904.



**ENDOMETRITIS.** Swabbing and irrigation with a solution of iodine (1 in 10) 1 part and glycerin 7 parts—R. Hobbs, *Brit. med. J.*, 11/1921, 35.

**EXOPHTHALMIC GOITRE** treated with 30 m. of a 10% alcoholic solution of iodine a day, increased in some cases to 60 m. or more—F R Fraser, *Lancet*, 1/1926, 551.

30 drops of Lugol's solution daily for 3 days, and 40 or 50 drops for one or two days. Hospitalisation is reduced to 5 days. Following operation, Lugol's solution is given by the mouth and by proctoclysis to combat hyperthyroidism—A S Jackson, *Lancet*, 1/1925, 759, 825; see also J W. McNee, *Lancet*, 1/1926, 551.

Maximum improvement after 2 to 6 weeks' treatment, when most cases relapse slowly and a low grade hyperthyroidism persists. Weight increased and B M R reduced to normal limits in 1 to 6 weeks, when it rises slowly again. 5 to 10 m. three times daily for first few weeks and 5 m. may be continued in some cases for 6 months, reducing dose on increase of symptoms. Dangerous with abnormally firm thyroid, exceptionally severe nervous symptoms, or loss of weight in first few weeks' treatment—L B. Cole, *Lancet*, 1/1927, 815.

A little solid iodine, say, 2 dr., should be placed in the dormitory in an open cup for youths up to the age of puberty, as they frequently suffer from defective action of the thyroid, but usually additional small doses of iodine are requisite—Sir James Barr, *Brit. med. J.*, 11/1927, 470.

New views on treatment of hyperthyroidism with iodine. Cases of thyrotoxic adenoma found in Belgium to react in the same manner to iodine as true exophthalmic goitre. Fractioning of the dose found efficacious—L Dautrebande, *Lancet*, 1/1929, 869; see also T. P. Dunhill, *ibid*, 949.

**LUPUS and PHTHISIS and LARYNGEAL TUBERCULOSIS** have been treated by evolving nascent iodine in the system. Potassium iodide 10 gr at 7 a.m. and followed 2 hours later by 1 oz. of chlorine water in  $\frac{1}{2}$  pint of lemonade. Later increased. Benefit in a week—J G Mackereth, *per Pharm. J.*, 1/1931, 569.

**MIDWIFERY.** The midwife needs an antiseptic which can be relied on to kill streptococci on the hands quickly—within 2 or 3 minutes at most—and without previous washing. Only iodine 0.5 to 1% and chloramine-T 1% do this—D L. Colebrook, *Lancet*, 11/1930, 369.

**RHEUMATOID ARTHRITIS** treatment. Iodine. Artificial pyrexia—A H Douthwaite, *Lancet*, 1/1931, 785.

**TONSILS.** Diseases of, due to fungi, well treated by application of dilute tincture of iodine and large doses of potassium iodide—as much as 30 gr thrice daily—Sir A. Castellani, *Prescriber*, 1930, 67.

**TUBERCULOUS ULCERS** and others treated by sodium iodide internally, 15 gr three times a day with hydrogen peroxide and a little acetic acid locally on cotton wool—S A. Pfannenstill, *Brit. med. J.*, 1/1925, 732.

It is generally agreed that patients with systemic disturbance, especially febrile cases, improve rapidly. The administration of minute amounts of iodine ( $\frac{1}{4}$  or  $\frac{1}{2}$  gr. every 5 days in butter-scotch) was found to give great improvement in pre-tubercular children when cod liver oil, etc., had failed. Chronic bronchitis and allied conditions also respond well—K Fraser, Cumberland, School M.O. Report, 1925.

**VARICOSE VEINS** treated by injecting 1% solution of iodine made with potassium iodide (Schiassi's method).—*Lancet*, 11/1922, 1288.

### Intravenous Iodine Injection.

#### EYE AFFECTIONS

For papillitis, retinitis pigmentosa, optic atrophy, or optic neuritis, treat root cause. Give iodine intravenously ( $\frac{1}{4}$  gr. each of iodine and potassium iodide in 10 ml. of distilled water) every 3 or 4 days up to 6 injections, rub mercurial ointment into the temples daily and give deep injections of  $\frac{1}{4}$  to 1 ml. of mercuric cyanide 1 in 2000 with procaine hydrochloride. Marked progress with this treatment, a notable feature being the rapidly improved vision after iodine injections. Where there are no prominent veins, the following is given intramuscularly—Sodium iodide 250 gr., iodine 200 gr., liquefied phenol 3 dr., distilled water 4000 ml., 10 ml. injected into gluteal muscles every 6 or 8 days. The mixture should not be stirred up.—E. R. Shett, *Brit. med. J.*, 11/1930, 1098.

**KALA-AZAR** treated by a solution containing iodine and potassium iodide, of each 6 gr., distilled water to 1 oz., approx. 1 gr. in 80 m. (5 ml.).—*Indian med Gaz.*, 1923, 312.

**PLAGUE** Early cases of bubonic plague well treated with iodine intravenously, 5 to 10 ml. daily for 4 days of solution of iodine 18 gr. and potassium iodide 36 gr in normal saline 4 oz., together with a mixture containing potassium iodide and stimulants, every 4 hours. Buboes treated by  $\frac{1}{8}$  gr. of mercuric chloride in 2 ml of water hypodermically in lymphatic area drained by groups of glands in which bubo formed.—*Indian med. Gaz.*, 1926, 63

**PNEUMONIA AND CELLULITIS** have been treated with initial dose of weak solution 20 m in 10 ml of normal saline, increased by 10 or 20 m., according to reaction, up to 60 m.—A. B. de Castro, *Indian med. Gaz.*, 1925, 141, and S. N. Datta, *ibid.*, 579. See also *J. trop. Med. (Hyg.)*, 1927, 225

**Pneumonia, erysipelas, cellulitis, rheumatism, septic wounds and bad cases of phagedenic ulcers** well treated. Iodine 24 gr., potassium iodide 36 gr., distilled water to 1 oz. *Dose*.—1 to 2 ml, diluted with 8 ml distilled water and given once or twice weekly.—E. Burke, *Brit med. J.*, 11/1927, 1062.

**PUERPERAL FEVER** Iodine intravenously "a most efficacious remedy,"  $\frac{1}{2}$  gr. in 2 ml. of water on 4 consecutive days.—S. R. Ingle, *Indian med. Gaz.*, 1926, 346 (1 gr. of potassium iodide needed to dissolve it)

**Balneum Iodi (B.P.C.).** Contains 4 oz. of strong solution of iodine per 30 gallons.

**Cataplasmata Iodi (B.P.C.).** Weak solution of iodine, 2 dr., in linseed poultice

[P1] **Chloroformum Iodi.** 1 in 30

Stains less and does not promote desquamation, itching or dermatitis like the alcoholic solution.

**Collodium Iodi (B.P.C.)** Iodine 6½% w/v in flexible collodion.

### **Glycerinum Iodi.**

Iodine 1, glycerin 50 Heat carefully until dissolved. A useful pigment; the skin does not harden by repeated application, nor peel off. Water helps solution, cf. Morton's Fluid.

For internal use this preparation is quite suitable diluted with water, with which it mixes temporarily. *Dose*.—On lines of the *Tinctura Iodi Fr. Cx.* method of use. It is approx.  $\frac{1}{2}$  the strength.

[P2] **Inhalatio Iodi Composita (L.H.).** *Dose*—10 minims on an oro-nasal mask

Creosote 2, phenol 2, spirit of chloroform 2, weak solution of iodine 1, spirit of ether 1.

For early pulmonary tuberculosis by inhalation from a "Burney Yeo" inhaler. *It must be continuous and in operation the whole of the 24 hours, excepting meal times* Six to 8 drops are used on the sponge of the inhaler every hour during the day, and two to three times during the night if awake. Non-irritating, beneficial and does not cause hemoptysis. Allays pyrexia and cough.

The antiseptics make their way into the pulmonary alveoli and the slow absorption of the anæsthetic solvents in a dilute condition carry with them the antiseptics into the blood and by the blood stream to the tuberculous foci. The alcohol must be considered as tonic and stimulating, as also the ether. The chloroform is locally sedative and reduces cough.

**Injectio Iodi (C.L.T.H.).** *Syn.* MORTON'S FLUID *Distinguish from the douche, which is also called "Injection."* Iodine 10 gr., potassium iodide 30 gr., water 25 m, dissolve and add glycerin to 1 oz. **Glycerin Iodi (St. T. H.)** is the same without the water.

In *spina bifida* 30 m. have been injected into the tumour, also into a soft solid goitre

**Injectio Iodi (C.H.W., L.H.).** **IODINE DOUCHE.** Weak solution of iodine 1 dr., water 1 pint. For injection in puerperal sepsis. Gangrene of the vulva, vagina and cervix has been treated by a douche of normal saline, cutting away the gangrenous parts, then giving a weak iodine douche, followed by packing with balsam of Peru gauze

**Injectio Iodi Fortissima.** *Dose.*—3 to 5 minims

Iodine 360 gr., potassium iodide 360 gr., distilled water 4½ dr. Measures exactly 1 oz. and contains ½ gr. of free iodine in each minim. For fibrous bronchocele.

A grain of iodine may be held in solution in a minim of fluid, by employing sodium iodide in the proportion of iodine 3, sodium iodide 2, and water q s. to 3 volumes.

**Insufflatio Iodi et Acidi Borici (Aural) U.C.H.**

Iodine 0.75, boric acid 99.25. Dissolve the iodine in alcohol and triturate with the boric acid.

**OTORRŒIA, CHRONIC.** Cures nearly 95% of chronic cases. The discharge is mopped or sucked out and the powder blown through the perforation into the middle ear until the deepest part of the meatus is full. The powder readily dissolves in the discharges within 48 hours.—R. Scott Stevenson, *Brit. med. J.*, i/1933, 95.

Insufflation of boric acid with 0.75% of iodine is more satisfactory than any other method. 96 cases treated with history of 4 weeks to 25 years—all dried up with from 1 to 30 treatments.—R. H. Bettington, *Med. J. Aust.*, 1935, 747.

**Iodum Oleatum.** (*Not for internal use.*)

An iodine-oleic acid compound containing 10% of iodine. When thoroughly rubbed into any part does not stain the skin, but is rapidly absorbed. Suitable for inflamed joints, enlarged scrofulous glands, skin affections, sciatica, sprains, chilblains; should prove of value in tinnitus aurium.

**Liquor Iodi Æthereus (B.P.C.).** *Syn.* TINCTURA IODI ÆTHÆREA. 2½% w/v in ether.

**Liquor Iodi Aquosus (B.P. Add.).** *Syn.* LUGOL'S SOLUTION, LIQUOR IODI COMPOSITUS.

*Dose.*—5 to 15 minims (0.3 to 1 ml.).

Iodine 5% w/v and potassium iodide 10% w/v in water. 15 m contains about ½ gr. of free I and about 2 gr. of total I.

B.P.C. is similar but has 5% w/v of each. *U.S.P. XI* is same as B.P. Add. with wider limits. *Average dose.*—3 minims

**Liquor Iodi Decoloratus (B.P.C.).** *Syn.* TINCTURA IODI DECOLORATA.

This solution contains ammonium iodide and ammonium iodate equivalent to about 3% w/v of iodine. A useful application for chilblains and for painting on exposed affected parts.

**Liquor Iodi Decoloratus Fortis** (*syn.* TINCTURA IODI DECOLORATA FORTIS) is occasionally ordered. It is prepared by dissolving iodine 2.85 g. in alcohol (90%) 27.5 ml., adding strong solution of ammonia 6.25 ml., and keeping in a warm place until decolorised.

**Liquor Iodi Fortis (B.P.).** *Syn.* TINCTURA IODI FORTIS, STRONG TINCTURE OF IODINE, PIGMENTUM IODI, LINIMENTUM IODI.

Contains 10% w/v of iodine and 6% w/v of potassium iodide in distilled water and alcohol 90%. Conforms with I.A.

**Solutio Iodi Spirituosa (P. Belg. IV and F.E. VIII)** is iodine 6.5 g., potassium iodide 2.5 g., alcohol (90%) 91 g.

**Tinctura Iodi (P.G. VI)** is iodine 7 g. and potassium iodide 3 g. dissolved in alcohol (90%) 90 g.

**Churchill's Tincture of Iodine.** Iodine 1200 gr. and potassium iodide ½ oz. dissolved in water 4 oz. and diluted with alcohol (90%) to 16 oz.

**Liquor Iodi Mitis (B.P.).** *Syn.* TINCTURA IODI MITIS, TINCTURA IODI, TINCTURE OF IODINE.

*Dose.*—5 to 30 minims (0.3 to 2 ml.).

Iodine 2½% *w/v*, and potassium iodide 1.5% *w/v*, in water and alcohol 90%.

### **Tinctura Iodi Mitis (U.S.P. XI).**

Iodine 2 and sodium iodide 2.3 in sufficient diluted alcohol (48.4 to 49.5% *v/v*) to make 100.

**Fatal dermatitis** following iodine spirit (2½% in industrial methylated spirit) for operation, sodium thiosulphate used to counteract. Pronounced idiosyncrasy no doubt.—R. C. Alexander, *Brit. med. J.*, 11/1930, 101.

Further cases.—D. G. De Bouk, *Brit. med. J.*, 11/1930, 162. A man applied Tinct. Iodi Mit to the arm for rheumatism. Caused a mass of blisters from head to foot. In bed 6 weeks.—L. Schapera, *ibid.*, 194.

Free application to the arms caused dermatitis. Vesicles turning to pustules. Temperature 103°F. Starch poultices used, also sodium bicarbonate, subsequently Lin. Calcis. Alcoholic iodine solutions are in their nature irritants. Their application to areas already denuded of surface protection open to risk.—O. Thomas Jones, *Brit. med. J.*, 1/1931, 15.

### **Coal Mines Regulations (First Aid) 1930, made by Board of Trade under Coal Mines Act, 1911, S. R. & O. 1930, No. 91.**

SECTION 8, UNDERGROUND ORGANISATION. Dressings, etc., to be provided and distributed by the owner.

Each person to carry a first-aid outfit of one large sterilised dressing, one small dressing and an ampoule of tincture of iodine (2% alcoholic), or other antiseptic approved by the B. of T., and securely packed.

#### **STERILISATION OF SKIN OF OPERATION AREAS.**

A 2½% solution in acetone-free industrial methylated spirit diluted to 70% strength has been used, also 1% in carbon tetrachloride (*Brit. med. J.*, 11/1930, 101) or 1.25% in 70% isopropyl alcohol (*Lancet*, 11/1928, 444).

### **Liquor Iodi Oleosus (B.P.C.). Syn. TINCTURA IODI OLEOSA.**

Iodine 8% *w/v* and castor oil 16½% *v/v* in alcohol 90%.

Repeatedly applied does not crack the skin as the tincture does.

**Iodine Sterules** (*Martindale, London*) are glass ampoules containing solution of iodine and encased in cotton wool and silk. On breaking the ampoule the solution is absorbed by the material which is then dabbed on to the part.

### **Liquor Iodi Simplex (B.P.).**

*Dose.*—3 to 15 minims (0.2 to 1 ml.), 15 m. contains about 1½ gr. of iodine. The dose may be gradually increased up to 25 or 30 m. thrice daily.

Iodine 9% *w/v*, in alcohol 95%. This corresponds to approximately 10% *w/w* and it is therefore the same strength as **Teinture d'Iode** (*Fr. Cx.* 1908) (also *P. Hung.*), sometimes called French tincture of iodine.

It is unfortunate, since the use of this preparation is in considerable vogue, that the above tincture of *Fr. Cx.* 1908 has been superseded by the **Teinture d'Iode iodurée** of *Fr. Cx. Supp.* 1920, the name of which was changed to **Teinture d'Iode officinale** in *Fr. Cx. Supp.* 1922 and confirmed in 1926. This preparation which is therefore now, strictly, the official French tincture of iodine, contains iodine 10 g., potassium iodide 4 g., alcohol 90% 136 g., but it is *not* the preparation usually required when French tincture is asked for in this country. Unless otherwise

directed *Liquor Iodi Simplex (B.P.)*, equivalent in strength to the original tincture of *Fr. Cx. 1908*, should be dispensed for "French Tincture of Iodine."

### *Uses and Prescribing Notes.*

This solution of iodine is given as a tonic before meals in tuberculosis. At the commencement of influenza and ordinary colds it is largely used on the Continent with excellent results. Small doses are invaluable in the vomiting of pregnancy, also in sea-sickness.

The "intensive iodine treatment" of tuberculosis was advised by L. Bourdreau. The treatment is also of value in arthritic cases, chronic gout and "rheumatic gout." *As much as 10 grains of iodine per diem can be given.* There may be slight catarrh of the nasal mucous membrane, but no iodism as from potassium iodide. The iodine is probably deposited on the stomach lining and slowly absorbed. The patient places the dose (15 drops equal approx. 10 minims) in a glass and adds half a tumbler of water. It may also be given in milk or as a mixture of equal volumes of simple tincture of iodine, spirit of chloroform and glycerin which form a clear solution containing 1 gr. of iodine in about 30 m.

Loss of free iodine is rapid during the first two months after manufacture but equilibrium is reached in about eight months with a total loss of about 20% of free iodine.

**Nebula Iodi Composita (B.P.C.).** Iodine 1% *w/v* and phenol  $\frac{1}{2}$ % *w/v* in light liquid paraffin.

**Nebula Iodi et Mentholis (B.P.C.)** Iodine 2% *w/v* and menthol 4% *w/v* in light liquid paraffin.

**Parogenum Iodi (B.P.C.).** *Syn.* IODINE VASOLIMENT, LINIMENTUM IODI PETROLATUM. 10% *w/v*

[P2] **Iodine-Medol (Creolinwerke, Hamburg)**, contains 1% of iodine and 5% of Creolin in a rapidly absorbed base. For chilblains, etc. Can be applied to denuded surfaces without producing escharotic effects.

**Iodinosol (Pearson, Mitcham)** Preparations containing 6% or 10% of iodine in a partly oxygenated mineral oil for use byunction. Also available in capsules containing 10 m. of the 6% preparation.

[P1] **Phenol Iodisatum (B.P.C.).** Iodine 10% *w/v* in liquefied phenol.

[P1-S1] **Pigmentum Iodi et Aconiti.** *Syn.* TINCTURA IODI ET ACONITI.

Weak tincture of iodine 1, tincture of aconite (Fleming's) 1. Periodontitis is relieved by iodine, or iodine and aconite pigment.

**Pigmentum Iodi Compositum (B.P.C.).** *Syn.* PIGMENTUM MANDL, MANDL'S PAINT.

Iodine  $1\frac{1}{2}$ % *w/v*, with potassium iodide and oil of peppermint, in a glycerin medium. It should be well shaken before use since the oil of peppermint is insoluble and rises to the surface on long standing. Used as a throat stimulant.

**Pigmentum Iodi et Ætheris Acetici (J. Dundas Grant)**  
Equal parts of simple solution of iodine, ethyl acetate and glycerin. This mixes quite well and is not unpleasant.

**Pigmentum Iodi cum Formaldehydo (M.H.).**

Solution of formaldehyde 10 m., weak solution of iodine 1 dr., oil of peppermint 2 m., glycerin to 1 oz. For granular pharyngitis

**Pigment. Iod. Fortis. (N.I.F.)**

Iodine 48 gr., potassium iodide 29 gr., boric acid  $9\frac{1}{2}$  gr., distilled water 48 m., chloroform 15 m., industrial methylated spirit to 1 oz.

**Pigment. Iod. Mit. (N.I.F.)** is similar, containing 12 gr. of iodine and 7 gr. of potassium iodide per oz.

**Pigment. Iod. (N.I.F.)** is a mixture of 130 m. of the strong paint and 350 m. of the weak. Contains about 4.5% w/v of iodine.

**Pigmentum Olei Picis cum Iodo (B.P.C.).** *Syn* PASTA IODI ET PICIS, COSTER'S PASTE.

Iodine 1 by weight dissolved with the aid of gentle heat in rectified oil of tar 4 by volume

**Uses.** For ringworm of the scalp; after well shaking the bottle the paint is well brushed in with a stiff brush. A scab will be produced which should be removed in a few days, the part cleansed by soaking with oil, and then soap and warm water; after drying, more paste should be applied. It seldom causes pain.

**Syrupus Iodotannicus (B.P.C.)**

*Dose* —  $\frac{1}{4}$  to 1 drachm (1 to 4 ml.)

Iodine and tannic acid, 1% w/w of each, in syrup and syrup of lemon

The *Fr. Cx*, *P. Ital. V*, *F.E. VIII*, *P. Belg. IV*, and *P. Ned. V* syrup is only  $\frac{1}{2}$  this strength, *viz.* 0.2% of iodine.

**Uses.** Of great value for enlarged glands in children and also as a tonic after removal of tonsils and adenoids. Suggested in lymphæmia, anæmia, dysmenorrhœa and pulmonary affections

Specially useful in cases of chronic lymphadenitis associated with or independent of adenoids. In atrophic rhinitis has given good results especially when combined with arsenic, also in simple bronchocele. In arteriosclerosis it is often more valuable than iodides or thyroid preparations.

**Syrupus Iodo-Tannicus (Martindale)**

*Dose.* —  $\frac{1}{4}$  to 2 drachms (2 to 8 ml.), containing  $\frac{1}{2}$  to 2  $\frac{1}{2}$  gr. of iodine, in water or wine.

Iodine 2, tannic acid 2, glycerin 20, water 30, syrup (with flavourings and carminatives) q.s. to 100.

**Syrupus Iodotannicus cum Phosphate (B.P.C.).**

*Dose.* —  $\frac{1}{4}$  to 1 drachm (1 to 4 ml.)

Contains about 2  $\frac{1}{2}$  gr. of calcium phosphate per dr. of iodotannic syrup.

**Syrupus Tann-Iodo-Phosphoratus (Martindale).**

*Dose.* —  $\frac{1}{4}$  to 2 drachms. Contains 5 gr. of monobasic calcium phosphate in 2 dr. of Syrupus Iodo-Tannicus (Martindale).

**Unguentum Iodi (B.P.C.).**

Iodine 4% with potassium iodide, in a simple ointment basis.

**Unguentum Iodi (U.S.P. XI).** Iodine 4, potassium iodide 4, glycerin 12, wool fat 5, yellow wax 5, petrolatum 70. It must contain from 6.5 to 7.5% of total iodine.

**Unguentum Iodi Denigrescens (B.P.C.)** contains iodine 5% in arachis oil and soft paraffin.

For use in rheumatic affections, enlarged glands, sprains, and syphilitic conditions.

### **Unguentum Iodi Intinctum.**

Iodine 1, oleic acid 4; heat to effect absorption and mix with yellow soft paraffin 14 and hard paraffin 1 previously melted together.

**Iodex** (*Menley & James, London*). A stainless iodine ointment containing 4% of iodine. Also made with methyl salicylate 5%. Suppositories are made equivalent to  $\frac{1}{2}$  gr. of iodine in a neutral base.

**Iodermiol** (*Hewlett, London*). An ointment containing about 5% of iodine which does not harden or discolour the skin. Also made with methyl salicylate [P2] **Vapor Iodi Æthereus** (*B.P.C.*). Ethereal solution of iodine 25% v/v, phenol 25% w/v, creosote 12.5% in alcohol 90% 10 m. to be used in an inhaler.

**Oleum Iodisatum** (*B.P.Add.*). *Syn. and Prop. Names.* OLEUM IODATUM (*U.S.P. XI*), IODATOL (*British Drug Houses, London*), IODINOL (*Martindale, London*), IODIPIN (*Merck, Darmstadt; Martindale, London*), LIPIODOL (*Guerbert, Paris; Bengué, London*), NEO-HYDRIOL (*Pharmaceutical Specialities (May & Baker) Ltd., London*), OLIOLASE (*Corbière, Paris; Anglo-French Drug Co., London*).

Iodised oil is an iodine-addition product of poppy-seed oil and may be prepared by treating poppy-seed oil with hydriodic acid. It is a colourless or pale yellow viscous oil with slightly alliaceous odour and contains 39 to 41% of combined iodine.

**Uses.** Iodised oil is employed for the X-ray diagnosis of bronchiectasis. For details of procedure, contraindications, etc., see Vol. II. It is also given internally when inorganic iodides disagree.

Weaker preparations, containing 10% or 25% of iodine, are also available under the above proprietary names. They are usually preferred to the 40% oil for internal administration, and can also be given hypodermically.

### **Sodium Ortho-iodohippurate.**

$C_6H_4I \cdot CONH \cdot CH_2COONa, 2H_2O = 363.0$ .

A white crystalline powder containing approximately 35% of I.

**Soluble** readily in water and alcohol.

**Uses.** Is used for intravenous, retrograde or oral pyelography. For intravenous use it is administered as a 50 to 60% solution in doses of 24 ml. for adults. For retrograde pyelography it is used in 15 to 30% solution. It may also be given orally in aqueous solution in doses of 180 grains (12 g.). Oral administration is usually less satisfactory except for children and when cystograms only are required. Following intravenous use, radiograms may be taken after about 10, 15 and 20 minutes. After oral administration pictures are usually taken in 1,  $1\frac{1}{2}$ , 2 and  $2\frac{1}{2}$  hours.

**Contraindications.** Hepatic disease, nephritis, uræmia, and iodine idiosyncrasy. It should not be administered orally to patients with any gastric lesion.

**Sterules Iodo-Ray** (*Martindale, London*) contain sodium o-iodohippurate in hypertonic dextrose solution. For intravenous administration they contain

10 g in 23 ml., and for retrograde use 3 g in 10 ml. The contents of the former may be given orally.

**Per-Abrodil** (*Bayer Products, London*). Known as **Diotrast** in U.S.A. A mixture or loose combination of 3:5-diiodo-4-pyridone-N-acetic acid,  $C_5H_4OHNI_2CH_2COOH$ , and diethanolamine,  $NH(CH_2CH_2OH)_2$ , in equimolecular proportions, used as a contrast medium for intravenous urography. Contains 51.8% of I and is supplied as a 35% w/v solution. *Dose*.—20 ml. of the solution warmed to body temperature injected into the cubital vein. X-ray photographs may be taken 10 minutes after the injection. Its use is contra-indicated in nephritis, hepatic disease and tuberculosis.

**Abrodil** (*Skiodan* in U.S.A.) is the sodium moniodomethylsulphonate, containing 52% of iodine. Supplied as a 20% solution. *Dose*.—2 g. per 15 lb. body weight for intravenous urography. For retrograde use 100 ml. of 10 or 20% solution is used. It is now largely replaced by the preceding compound.

**Tenebryl** (*Bengué, London*) is sodium diiodomethanesulphonate for intravenous urography. *Dose*—15 g. in 75 ml. of water.

**Uroselectan B** (*Schering, London*). Known as **Neo-Iopax** in U.S.A. Di-sodium salt of 3:5-diiodo-4-pyridoxyl-N-methyl-2'6-dicarboxylic acid, containing 51.5% of I, used in pyelography. Ampoules contain 15 g in 20 ml. of 10% aqueous invert sugar solution.

*Dose*—20 ml. intravenously (less for children) warmed to 100°F. Stated to be well tolerated.

For anatomical information only, a single pyelogram 20 to 30 minutes after the injection suffices, but for urological purposes exposures are made at 10, 30, and 50 minutes. Before the second and third exposure the bladder should be emptied. When renal function is normal the best films are often obtained in 2 to 5 minutes after injection, with function abnormal the best results may not be obtained for 6 to 24 hours, and if function is completely suspended it is impossible to obtain a pyelogram.

To be used with caution in patients with severely impaired liver function or acute or chronic uræmia, and where the urinary disease is accompanied by severe general disease.

The substance was preceded by Uroselectan without the suffix "B," the sodium salt of 2-oxo-5-iodo-pyridine-N-acetic acid. This was employed in strength of 40 g. in 100 ml. of warm water intravenously.

Uroselectan B, in excretion urography. Non-toxic and rapidly eliminated in a concentrated form. Small dose—Prof. v. Lichtenberg, *Brit. med. J.*, 1/1931, 625, 633.

Recent advances in diagnostic methods in renal affections. Technique of injection of Uroselectan B and Abrodil—R. Ogier Ward, *Brit med J.*, ii/1931, 175, Roy. Soc. Med. Discussion—*Lancet*, i/1931, 757, 767.

The indications for intravenous urography in children are much the same as for adults. For children of 5 to 7 years give one-third the adult dose, with a reduction for younger children, but never less than a quarter of the adult dose. First film taken within 10 minutes and further films at 30 and 50 minutes after injection. To prevent gas collection in the alimentary tract (common in children) give Pulv. Glycyrrhizæ Co. 48 hours before injection, and, if possible, have child up and about. With the Lysholm Fixed Bucky grid, exposures can be made in a fraction of a second. No untoward reactions. For the first time a practical routine method is provided for visualising the upper urinary tract in children.—C. G. Teall, *Brit. med. J.*, ii/1932, 788.

*Infusion urography* (injection of opaque media *per urethram* through a catheter) and *excretion urography* (injection into the circulating blood of a chemical substance rapidly excreted in the urine) are not in opposition but are complementary. Infusion urography is an anatomical demonstration revealing form, while excretion urography reveals function.—Henry Wade, *Brit med. J.*, i/1933, 353.

## IODINE COMPOUNDS FOR INTERNAL USE

The following preparations containing organic compounds of iodine are given internally in place of the inorganic iodides for all conditions in which the latter are indicated. The organic compounds are stated to be better tolerated and less likely to produce



iodism. They are administered in syphilis, actinomycosis, goitre, arthritis, bronchial asthma, scrofula, etc.

**Calcii Iodobehenas** (U.S.P. XI).  $(C_{21}H_{43}ICOO)_2Ca$  *Prop. Name.* SAJODIN (Bayer Products, London). *Dose.*—5 to 15 grains (0.3 to 1 g.) up to 90 grains per diem after meals. U.S.P. XI average dose 8 grains. A tasteless powder containing not less than 23.5% of I. Insoluble in water.

**Iodo-Casein.** *Dose.*—10 to 15 grains (0.6 to 1 g.).

A yellowish brown powder containing 15% of I, used as a substitute for inorganic iodides. Insoluble in acid, and partially dissolved in alkaline solutions.

**Iodicin** (Burroughs Wellcome, London). A calcium salt of iodicinoleic acid, containing 20% of I, in capsules containing the equivalent of 1 gr of iodine (*dose.*—1 to 3, 3 or 4 times daily) and also in chocolate tablets containing the equivalent of  $\frac{1}{2}$  gr of iodine (*dose.*—1 weekly to 1 daily) for goitre.

**Iodalbin** (Parke, Davis, London). An iodo-protein compound containing 21.5% of I. *Average dose.*—5 grains after meals.

**Iodival** (Knoll, Ludwigshafen; Pharmaceutical Products, London).

$\alpha$ -Monoiodoisovalerylcarbamide. Contains 40% of I. *Dose.*—1 5-grain tablet 3 times daily.

**Iodoprotein** (Martindale, London). A brown powder containing about 10% of I. Also available in 5 and 10-gr. tablets. *Dose.*—10 to 15 grains (0.6 to 1 g.), or more if desired.

**Iodo-Scilline** (Anglo-French Drug Co., London). Iodopeptone 0.01 g., powdered squill 0.02 g., scammony resin 0.02 g. in each pill. *Dose.*—2 to 6 pills daily.

**Iodostarin** (Hoffmann-La Roche, London).

Di-iodotarinic acid,  $CH_3(CH_2)_{10}Cl\ Cl(CH_2)_4COOH = 534.1$ , in 3-gr tablets. It contains 47.5% of I. *Dose.*—1 to 4 tablets thrice daily. Tablets containing 5 mg. of Iodostarin are available for the prophylaxis and treatment of endemic goitre.

**Iolase** (Anglo-French Drug Co., London). Combination of iodine with yeast albumoses (10% I) in solution.

**Lipoliodine-Ciba** (Ciba, London). The ethyl ester of di-iodobrassicic acid, containing over 40% of I. Tablets contain 0.3 g. To be taken (in place of the inorganic iodides) after the chief meals, masticating thoroughly.

**Oridine** (Lilly, London). Iodine in organic combination with fatty acids in chocolate tablets, each containing  $\frac{1}{2}$  gr. of iodine. *Dose.*—Prophylactic, 1 or 2 tablets until 40 are taken, treatment, 2 or 3 daily over a considerable period.

**Seroden Capsules** (Allen & Hanburys, London). Gelatin capsules containing 1 gr of iodine in combination with serum proteins. *Dose.*—1 to 3 capsules 2 or 3 times daily.

### IODINE COMPOUNDS FOR INJECTION.

**Entodon** (Bayer Products, London). A 20% solution of hexamethyldiamino-isopropanol biniodide (1 ml. contains 0.118 g of I). *Dose.*—2 ml daily or every second or third day, by subcutaneous, intramuscular or intravenous injection. In syphilis, atheroma, angina pectoris, bronchial asthma, emphysema, etc.

**Iodaseptine** (Anglo-French Drug Co., London). Iodobenzomethylformine (formed by combination of iodine with formaldehyde and the phenyl radicle from benzomethyl ether) in ampoules for intramuscular or intravenous injection, or drops for oral use. An internal antiseptic in chronic bacterial infections.

**Septicemine** (Anglo-French Drug Co., London). Iodobenzomethylformine. A combination of iodine and formaldehyde similar to Iodaseptine (*q.v.*) but containing a lower percentage of iodine (33%) and more formaldehyde. *Dose.*—In acute infections, from 1 to 4 intravenous injections of 4 ml., in subacute infections, 4 ml. during 24 or 48 hours. In septicæmia and all acute infections.

### Colloidal Iodine.

Colloidal iodine solution may be prepared by acting upon sodium iodide with sodium nitrite in acid dextrose solution. The nitric oxide evolved must be removed. The usual strength is 1 in 2000.

**Dose**—1 to 4 drachms (4 to 16 ml.) *per os*. Commercial preparations are frequently solutions containing iodine in combination with proteins. Colloidal solutions are administered in place of inorganic iodides.

**Alphidine** (*Oppenheimer, London*) Preparations stated to contain a new and probably allotropic form of iodine giving a colloidal solution in water. It is non-toxic on internal administration. Is available in chocolate-coated tablets containing  $\frac{1}{2}$  gr. of iodine, in solution (0.4%), and as a non-staining cream containing 1% in a non-greasy base.

**Collosol Iodine** (*British Colloids, London*) is available in aqueous solution paste, ointment or oily solution.

**Iodeol** (*Bengué, London*) Electrically prepared colloidal solution of iodine in oil for intramuscular injection in doses of 1 ml. containing 0.2 g. of I. Used in pulmonary and rheumatic affections. Also available in capsules (= 0.25 g. of I) and suppositories.

**Iodargol** (*Bengué, London*) is a similar preparation containing 0.4 g. of I per dose, for urethral injection in infections of the urinary tract.

## IPECACUANHA

B P, U S P XI, P. G. VI, P. Hek V, P. Dan, etc

Syn. IPECAC.

[P1] "*Alkaloids, the following; their salts, simple or complex—Emetine.*"

[S1] "*Alkaloids, the following; their salts, simple or complex.—Emetine except substances containing less than 1% of emetine*"

[S3] "*Alkaloids—Emetine—in Ipecacuanha; extracts and tinctures of ipecacuanha; substances containing less than 0.05% of emetine*"

The dried root of *Cephaelis Ipecacuanha* (syn. *Uragoga Ipecacuanha*) (Rubiaceæ) from Brazil, containing not less than 2% of total alkaloids. The commonest variety is known as Rio ipecacuanha. A second variety is the Minas ipecacuanha also from Brazil. Other varieties are the Indian and Johore from the same plant, grown in Straits Settlements. They contain about 2 to 3% of total alkaloids of which about 60 to 70% is emetine. Cartagena ipecacuanha, from *Psychotria acuminata*, is not official, about 30 to 40% of the total alkaloids is emetine. It is thicker, the annulations less marked (taking the form of narrow merging ridges) and its starch-grains are somewhat larger. U.S.P. XI allows both *Cephaelis Ipecacuanha* (Rio) and *C. acuminata* (Cartagena) if yielding not less than 2% of ether-soluble alkaloids.

When ipecacuanha is prescribed Ipecacuanha Pulverata must be dispensed.

**Antidotes.** Emetics probably unnecessary as patient usually vomits. Give large doses of medicinal charcoal, stirred up in water. Keep patient lying down and quiet. When vomiting ceases, stimulants may be given. Morphine,  $\frac{1}{2}$  gr. hypodermically, if required.

**Uses.** Expectorant, emetic. If taken in sufficiently large doses it is not its own antidote. Loosens phlegm, *e.g.*, in bronchitis, whooping-cough and croup. In small doses is stomachic and increases the flow of bile. The alkaloid emetine contained in it has been found to be virtually a specific for amœbic dysentery. Frequent doses, 1 to 2 minims of the tincture, sometimes check sickness.

For tropical liver abscess ipecacuanha is specific. It cures the active or latent dysentery which has caused the suppurative hepatitis and prevents further breaking down of the liver substance. Large doses better than several small ones. Vomiting may be prevented by chloral hydrate and *Liquor Morphinæ*.

Diarrhœa is well treated by 0.8 to 1 g. of the powdered root, *p d.*, divided into 5 or 6 doses of 0.2 g. Each dose is taken in a warm infusion every two hours. The remedy is well tolerated; it sometimes gives rise to nausea, but rarely to vomiting.

**Acetum Ipecacuanhæ (B.P.C.).**

**Dose.**—10 to 30 minims (0.6 to 2 ml.).

Contains 5% *v/v* of liquid extract of ipecacuanha in alcohol, water and acetic acid. Alkaloidal content, 0.1%.

[P1 81] **Applicatus Arsenicalis Composita (Gt. Orm. H.).**

Solution of arsenious oxide 2 dr., tincture of ipecacuanha 2 dr., glycerin 2 dr., peppermint water to 1 oz. For application to the tongue and gums dilute 3 drops with  $\frac{1}{2}$  dr. of water and use on a piece of gauze.

[P1-81] **Collutorium Arsenicalis (G. Sg. H.).**

Tincture of ipecacuanha 3 dr., glycerin 5 dr., arsenical solution 5 dr., hydrogen peroxide 5 oz., water to 8 oz. Used diluted with an equal quantity of water for Vincent's angina.

**Elixir Ipecacuanhæ (B.P.C.).**

**Dose.**—10 to 30 minims (0.6 to 2 ml.).

Contains 5% *v/v* of liquid extract of ipecacuanha in a flavoured basis. Alkaloidal content, 0.1%.

**Extractum Ipecacuanhæ (Fr. Cx.).** Extract the root with 70% alcohol, and evaporate to a firm extract.

The water-soluble extractive under the name **Emetin** has been administered in pills or solution as an expectorant in doses of  $\frac{1}{16}$  to  $\frac{1}{10}$  grain (0.004 to 0.006 g.) and as an emetic in doses of  $\frac{1}{2}$  to 1 grain (0.03 to 0.06 g.).

**Extractum Ipecacuanhæ Liquidum (B.P.).**

**Dose.**— $\frac{1}{2}$  to 2 minims (0.03 to 0.12 ml.), emetic dose, 10 to 30 minims (0.6 to 2 ml.). 2 minims contains  $\frac{1}{25}$  gr. of total alkaloids calculated as emetine.

**Fluidextractum Ipecacuanhæ (U.S.P. XI).** *Average dose.*—Expectorant, 1 minim (0.06 ml.); emetic, 15 minims (1 ml.).

Contains 28 to 33% of alcohol, and hydrochloric acid, and also differs from *B.P.* liquid extract by being standardised to 2% of ether-soluble alkaloids instead of total alkaloids. *P. Helv. V* has liquid extract containing "at least 2% emetine and cephaeline"

[P1 81] **Ipecacuanha Pulverata (B.P.).** *Syn.* PULVIS IPECACUANHÆ. **Dose.**— $\frac{1}{2}$  to 2 grains (0.03 to 0.12 g.); emetic dose, 15 to 30

grains (1 to 2 g.) 2 grains contains about  $\frac{1}{25}$  gr. of total alkaloids.

Ipecacuanha in fine powder adjusted by admixture with stronger or weaker powder, or lactose, to contain 2% of total alkaloids calculated as emetine, of which not less than two-thirds consists of non-phenolic alkaloids calculated as emetine.

[P1] **Mist. Expect.** (*N I F.*). Ammonium carbonate 3 gr., tincture of ipecacuanha  $7\frac{1}{2}$  m, camphorated tincture of opium 15 m., water to  $\frac{1}{2}$  oz.

**Mistura Expectorans** (*St. T. H.*). *Dose*—For adults, 1 oz; for infants, 1 to 2 drachms.

Dilute solution of ammonium acetate 2 dr., vinegar of squill 15 m, tincture of ipecacuanha 15 m, glycerin 40 m, chloroform water to 1 oz

**Mistura Ipecacuanhæ Composita** (*B.P.C.*) *Syn* MISTURA EXPECTORANS. *Dose*.— $\frac{1}{2}$  to 1 ounce (15 to 30 ml.).

Contains vinegar of ipecacuanha 24 m and strong solution of ammonium acetate 15 m. with oxymel of squill, glycerin and chloroform water to 1 oz.

**Mist. Ipecac. c. Scill.** (*N I F.*). Liquid extract of ipecacuanha  $\frac{1}{2}$  m, liquid extract of squill 2 m, concentrated solution of ethyl nitrite  $2\frac{1}{2}$  m (equivalent to spirit of ethyl nitrite 20 m), water to  $\frac{1}{2}$  oz

[P1] **Mistura Ipecacuanhæ Salina** (*Gt. Orm. H.*). (*Dose* for 1 year old child)

Camphorated tincture of opium 2 m, tincture of ipecacuanha  $1\frac{1}{2}$  m, spirit of nitrous ether 4 m, solution of ammonium acetate 15 m, syrup of tolu 4 m, water to 1 dr.

[P1] **Mistura Pertussis** (*St. T. H.*). Tincture of belladonna 5 m, tincture of ipecacuanha 5 m, syrup of tolu 30 m, cinnamon water to 1 dr *Dose*— $\frac{1}{2}$  to 1 drachm.

[P1 81] **Pigmentum Ipecacuanhæ et Arsenici** (*R F H*)

Tincture of ipecacuanha 2 dr., arsenical solution 2 dr, glycerin 2 dr, water to 1 oz. For a child dilute 5 m to 1 oz of water and rub into the gums, increase strength if child can be taught to expectorate For use in pyorrhœa. To be painted on the ulceration. *A drop or two only to be used.*

[P1 81] **Pilulæ Ipecacuanhæ cum Scilla** (*B P.C.*). *Dose*.—1 or 2 pills. Each pill contains 2 gr. of Dover's powder and  $\frac{3}{8}$  gr. each of squill and ammoniacum (*exempt* [D]).

[P1 81] **Pulvis Ipecacuanhæ et Opii** (*B P, U.S.P. XI.*) *Syn.* PULVIS OPII ET IPECACUANHÆ COMPOSITUS (*I.A.*), PULVIS IPECACUANHÆ COMPOSITUS, DOVER'S POWDER, PULVIS OPII COMPOSITUS (*P. Ned. V.*).

*Dose*.—5 to 10 grains (0.3 to 0.6 g). 10 grains contain  $\frac{1}{10}$  gr. of anhydrous morphine.

Contains 10% each of powdered ipecacuanha and powdered opium, with lactose (*exempt* [D]) Is diaphoretic and anodyne; for an acute catarrh or coryza take 10 gr. at bedtime followed at once by a hot drink and 5 gr. of quinine next morning.

[D-P1-81] **Poudre d'ipecacuanha opiacée** (*Fr. Cx.*). *Max. single dose* 15 grains, max. during 24 hours 60 grains Is the same but has equal parts of potassium nitrate and potassium sulphate *vice* lactose.

**Syrupus Ipecacuanhæ** (*B.P.C.*).

*Dose*.— $\frac{1}{2}$  to 2 drachms (2 to 8 ml.). Contains 50% v/v of vinegar of ipecacuanha.

*P.G. VI* and *I.A.* have *ipecacuanha* tincture 1, syrup 9.

*Fr. Cx.* has "Sirop" 1% of extract made by dissolving extract 1 in alcohol 70% 3, and mixing with syrup 100; intended as an emetic. That of *I.A.* is not emetic in usual doses.

**Syrupus Ipecacuanhæ** (*U S P XI*) *Average dose.*—Expectorant, 12 minims (0.75 ml.); emetic, 4 drachms (15 ml.)

Fluid extract of *ipecacuanha* 7, glycerin 10, syrup to 100.

**Tincture Ipecacuanhæ** (*B P.*).

*Dose.*—10 to 30 minims (0.6 to 2 ml.), emetic dose,  $\frac{1}{2}$  to 1 ounce (15 to 30 ml.). 30 minims contains about  $\frac{1}{7}$  gr. of alkaloids

Prepared with 5% *v/v* of liquid extract in a glycerin-alcohol-water medium and contains 0.1% *w/v* of alkaloids *B.P. Add.* requires the addition of 1.65% *v/v* (1 m. per dr) of acetic acid. It is the same strength as *Vinum Ipecacuanhæ* (*B P '14*), which was prepared with sherry. The *B.P.* requires the tincture to be dispensed when the *Vinum* is prescribed.

*Fr. Cx.*, *P.G. VI*, *P. Belg. IV*, *P. Hung* and *I.A.* include a tincture (10%) made by percolation of the root with alcohol 70%. *P.G. VI* is standardised to contain 0.194% of emetine.

**Trochisci Ipecacuanhæ** (*B P C*) contain  $\frac{1}{4}$  gr (0.015 g) in each, with simple basis.

[P1] **Trochisci Morphine et Emetini** (*TROCHISCI TUSSES*) contain morphine  $\frac{1}{10}$  gr. with emetine  $\frac{1}{10}$  gr. In bronchial asthma.

[P1] **Unguentum Ipecacuanhæ et Crotonis.** *Pulvis Ipecacuanha* 1, *Lini-mentum Crotonis* 1, *Adeps Benzoinatus* 2. A powerful counter-irritant, rubbed on the skin of epigastrium relieves gastralgia.

[P1] **Alcresta Tablets of Ipecac** (*Lilly, London*) Uncoated tablets representing an adsorption compound of ipecac alkaloids with a form of aluminium silicate. The compound passes through the stomach unchanged and liberates the alkaloids in the intestinal tract. Each tablet contains the alkaloids from 10 gr. of *ipecacuanha* (*U S P XI*)

[P1] **Ipecopan** (*Sandoz, London, Brooks & Warburton, London*) Malted tablets representing the alkaloids of Dover's powder, free from cephaeline. *Dose.*—1 to 3 tablets thrice daily. For treatment of coughs

[P1-81] **Emetina.** *Syn* IPECINE, METHYLCEPHAELINE.

$C_{29}H_{40}O_4N_2 = 480.3$  *Dose.*— $\frac{1}{11}$  to 1 grain (0.005 to 0.06 g)

A white powder darkening on exposure. In the stable neutral salts the bases are combined with two equivalents of acid. Basic salts also exist

**Soluble** in water 1 in 600 at 15.5°, 1 in 900 at 40°. Soluble also in ether, alcohol, chloroform and fixed oils. Insoluble in essential oils.

1 gr. in 6 dr. of olive oil has been given as an enema for amœbic dysentery.

[P1] **Emetol** (*Martindale, London*). A solution of emetine base 1 gr. in 2 dr (8 ml.) of olive oil, for rectal use in amœbic dysentery. See *Edn XIX*, p. 535. *Dose.*—2 drachms are added to 4 or 6 dr of ether and 8 oz (230 ml) of olive oil for use.

[P1 81] **Emetine Hydrobromide.**  $C_{29}H_{40}O_4N_2 \cdot 2HBr \cdot 4H_2O = 714.2$ . *Dose.*—As for hydrochloride, *q.v.* for details.

White crystalline salt. Soluble about 1 in 70 only of water, hence the hydrochloride should be prescribed in preference. The addition of a little hydrobromic acid does not affect solubility.

[P1-61] **Emetinæ Hydrochloridum** (B.P., P. Jap. IV, Fr. Ca Supp. II, P.G. VI).  $C_{20}H_{40}O_4N_2 \cdot 2HCl \cdot 7H_2O = 679.4$ .

P. Ned V has "varying quantity" of water P. Helv. V has "about  $4H_2O$ ." P. Ital. V allows 20% and F.E. VIII 19% of moisture. P. Belg. IV is anhydrous.

**Dose.**— $\frac{1}{2}$  to 1 grain (0.03 to 0.06 g.) by injection,  $\frac{1}{10}$  to  $\frac{1}{5}$  grain (0.0006 to 0.0025 g.) *per os* as an expectorant, but larger doses, e.g.,  $\frac{1}{4}$ ,  $\frac{1}{2}$  grain are given in enteric coated tablets or pills in amœbic dysentery. As an emetic *per os*  $\frac{1}{10}$  to  $\frac{1}{8}$  grain (0.005 to 0.01 g.) has been given. Intravenously  $\frac{1}{2}$  to  $\frac{3}{4}$  grain in 5 ml. of normal saline has been given.

Fr. Cx. Supp. has maximum dose 0.1 g. per dose and per diem P. Jap. 0.05 and 0.15 g. respectively P. Helv. V 0.1 and 0.2 g.

**Soluble** about 1 in 9 in water, but this is not permanent at  $15.5^\circ$ —it is safer to use 20 parts of water at least. The addition of hydrochloric acid throws out the acid salt which is less soluble. Also soluble in alcohol 90%.

Injections made with distilled water are less irritant than those made with normal saline. Solutions in ampoules stand sterilising. —*Yearb. Pharm*, 1919, 12

**Cumulative Action.** There is a possibility of this from long use, but there have been very few reports of its occurrence.

A single dose should not exceed 1 mg per kilo (i.e., 1 gr for a man) and total dose 10 mg per kilo. It is slowly excreted and is cumulative.—H. H. Anderson and C. D. Leake, *per Med Annu*, 1931, 17

**Antidotes.** Treat as for poisoning by ipecacuanha, *see* p. 597.

**Uses.** The standard treatment for amœbic dysentery. It kills the amœbæ or active living forms which are present in the tissues of the bowel but does not kill the cystic stage. It has also been successfully used in bilharziasis, cholera, Guinea worm, and oriental sore. Morphine habit (*qv*) has been treated, and also alcoholism. Injections of 1 gr. are often effective in arresting hæmoptysis. A solution of emetine hydrochloride  $\frac{1}{2}$  gr. in 8 oz. of water has been advocated as a mouth-wash in pyorrhœa.

### Treatment of Amœbic Dysentery.

When amœbæ are taken fresh and vigorous from dysenteric ulcers in the bowel, emetine has only a weak action on them. Prof. Dixon (*Brit. med J.*, 11/1922, 410) maintained that "Emetine does not kill the amœbæ except in the human body," but Dobell and Laird (*Parasitology*, June, 1926, *Lancet*, 11/1926, 762) conclude that the alkaloid kills *E. histolytica* by direct action. They conclude further that 1 in 50,000 is the highest concentration of emetine that the amœba will tolerate for more than a short time—this is the threshold value of emetine. It is 10 times more toxic than acetarsol. The poisoning process of emetine is slow. A very small amount constantly present in the intestine for days or weeks would probably suffice to make life for *E. histolytica* (though not *E. coli*) impossible.

Treatment usually consists of a combination of hypodermic or intramuscular injection of emetine hydrochloride with oral

administration of one of the less irritant compounds such as emetine bismuth iodide or the periodide. The injections are made twice daily, an average dose being  $\frac{1}{2}$  gr. each time until 10 to 12 gr. has been given. The treatment is, however, only successful in about one third of the cases treated. The relative failure of hypodermic injections in the treatment of dysentery carriers is probably explained by the entamœbæ being more or less shut off from the circulation and tissue fluids of the patient. Re-treatment with equal or larger amounts is rarely successful.

Emetine is more efficacious in amœbic lesions of the liver in extirpating *Entamœba histolytica* than when the parasite invades the bowel wall. Cases recorded show that emetine should be used only as an adjuvant to surgical measures, e.g., aspiration —P. Manson-Bahr and R. M. Morris, *Lancet*, 1/1926, 69.

This does not agree with previous statements —See *ibid*, 156.

Emetine alone is sufficient to cure cases of liver abscess. Pain and inconvenience of aspiration undesirable —V. S. Hodson, *Lancet*, 1/1926, 681. Manson-Bahr's reply *ibid*.

Aspiration plus emetine cures hepatic abscess in the most certain way possible. After an injection of cocaine, removal of pus relieves the patient —E. Owen Thurston, *Lancet*, 1/1926, 784.

From observations on the use of emetine in 554 cases of amœbiasis over a period of 15 years at the Mayo Clinic, it seems hardly justifiable to discard its use, though it should be re-emphasised that in the total dose of 0.65 g. in two weeks, it is employed only to control acute manifestations of the disease and to give the patient prompt relief, but not with the idea of continuing the drug to bring about a cure —P. W. Brown, *J. Amer. med. Ass.*, 11/1935, 1321.

It is now recognised that emetine possesses so great a therapeutic hazard in dosage required for effectiveness in amœbiasis that its routine clinical use in this disease is no longer justified. It has recently been demonstrated *in vitro* that amounts of emetine which are directly lethal for amœbæ are much greater than the body tissues can tolerate. It is a fact that clinically safe doses are not always sufficient to rid the patient of this infection, and that amounts in excess of 10 gr. total may produce permanent cardiac damage. The use of this alkaloid should be confined to amœbic hepatitis or abscess and to complicated amœbiasis requiring surgical intervention, since other less harmful drugs are now available for the average uncomplicated case. When emetine is used, one should record the blood pressure and pulse-rate daily. A lowering of pressure and an increase in pulse-rate may indicate impending cardiac damage —H. A. Anderson, *J. trop. Med. (Hyg.)*, 1935, 271.

#### EMETINE INJECTIONS IN CONJUNCTION WITH ARSENIC ORALLY

Acetarsol 4 gr. twice daily is given for a week or 10 days in conjunction with daily injections of emetine hydrochloride 1 gr.

At the Mayo Clinic, if the patient has not received anti-amœbic treatment recently he is given 0.065 g. of emetine hydrochloride subcutaneously, twice daily for three days. After an interval of a week 0.043 g. of emetine is given twice daily for three more days. With the institution of the emetine, Treparsol 0.25 g. is administered orally with each meal for four days. If there is no intolerance to arsenic, two more such courses are prescribed, with intervals of ten days between the courses. If the patient is quite ill he is kept in bed for the first few days. Obviously, the diet may need to be bland and simple if there is much dysentery, but within 24 to 48 hours a full and generous diet is begun. A rich, high-vitamin diet has a profound influence on the healing of amœbic ulceration. Hepatic involvement may subside, but if there is a large collection of broken-down material, aspiration preferably, or occasionally open drainage, may be required. If stool tests are positive following this regimen, three courses of chiniofon are prescribed: 3 g. orally per day for a week, and repeated for two more such courses with a week's interval between courses. If diarrhoea is increased, the daily dose is decreased, thereby prolonging each course. Failure after this would indicate a course of 1 injection of arsphenamine weekly for 6 weeks, and 1 dr. (3.88 g.) of bismuth subnitrate from 3 to 6 times

daily during the period. A "cure" should not be regarded as having been attained until three faecal specimens monthly, obtained preferably after a saline purge, are negative over a period of six months.—P. W. Brown, *J. Amer. med. Ass.*, ii/1935, 1319

Arsphenamine and emetine a useful combination—persist with resistant cases.—*J. Amer. med. Ass.*, i/1926, 457.

Arsphenamine 0.1 g. tablets, 2 to 6 daily, found efficacious cysts destroyed, —*Pr. méd.*, Apr., 1926, 497.

Treparsol, 4 tablets daily, has been used —*Prescriber*, 1927, 15

### EMETINE INJECTIONS IN CONJUNCTION WITH BISMUTH ORALLY (JAMES AND DEEKS).

Emetine hydrochloride is injected hypodermically in doses of  $\frac{1}{2}$  to 3 gr. to the limit of tolerance and bismuth subnitrate ("Panama bismuth") is given orally, a heaped teaspoonful (180 gr.) in a tumbler of water every 3 hours night and day in severe cases. In chronic cases continue for 2 to 3 months after convalescence with 3 or 4 doses daily. Cyanosis and tachycardia may occur but have been stated to be due to impurities in the bismuth subnitrate.

BILHARZIASIS. As much as 0.12 g. (single dose) given intravenously in bilharzia. 10 to 12 injections at 3 to 5 day intervals will cure, the total amount given being from 0.85 to 1.05 g.—Diamantis, *Brit. med. J.*, i/1921, 70 See also *Brit. med. J. Epit.*, i/1920, 33.

Four 3-grain doses every third day intramuscularly sufficient A child will stand 2  $\frac{1}{2}$  grains—"B. H.," *Brit. med. J.*, i/1921, 586

Commence with  $\frac{1}{2}$  grain initially intramuscularly for an adult and  $\frac{1}{4}$  grain for a child and work up to 1 grain for a child of 12. Injections generally given daily for 3 days, and then 3 times a week for 3 weeks Iron and arsenic as tonic—F. G. Cawston, *Lancet*, ii/1921, 1049

Japanese bilharzia disease well treated by emetine, but there may be severe cardiac depression.—F. G. Cawston, *Brit. med. J.*, ii/1921, 1031.

Emetine hydrochloride  $\frac{1}{2}$  to  $\frac{1}{4}$  gr in 1% phenol solution intramuscularly on alternate days eradicates permanently.—F. G. Cawston, *J. trop. Med. (Hyg.)*, 1922, 112.

BRONCHOPNEUMONIA in children Though not a specific, it is of value, the febrile period is shortened and the stomach is left free from irritation by expectorants. *Daily hypodermic injection*—up to 4 years,  $\frac{1}{4}$  grain 4 to 10 years  $\frac{1}{2}$  grain 10 to 15,  $\frac{1}{2}$  grain. Discontinue if no definite results after 6 injections—C. R. Wilson, *Brit. med. J.*, i/1928, 845.

GASTRIC ULCER Over 400 cases of gastric and duodenal ulceration treated by intravenous injections; relief complete in each case in periods ranging from 3 days to a week. 1 grain of the salt is dissolved in 6 ml. of treble distilled water and 1 injection into the median basilic or cephalic vein is given on alternate days until 6 have been administered, followed by an interval of a week, when the injections can be repeated. Injections given on an empty stomach and the patient should be kept on a bland salt-free diet during treatment, alcohol in any form being strictly prohibited.—A. E. Olpp, *Med. Rec.*, 1934, 472.

GUINEA WORM. 17 cases treated successfully by emetine given intravenously and *per os*.—E. Tournier, per *J. trop. Med. (Hyg.)*, 1923, 101.

ORIENTAL SORE. 2 cases cured in 3 weeks by 2 injections of emetine hydrochloride.—Caliceti, per *J. trop. Med. (Hyg.)*, 1923, 201.

PULMONARY SUPPURATION. Emetine 1 gr. daily for 8 to 12 days, preferably combined with strychnine, of benefit. In some cases dramatic results, in others of no value, but never known to do harm—A. J. Scott Pinchin and H. V. Morlock, *Lancet*, ii/1930, 842, *Practitioner*, ii/1931, 345.

RHEUMATISM, acute articular, resistant to all other forms of treatment, cured by emetine.—Trolli, per *J. trop. Med. (Hyg.)*, 1923, 149.

### [P1 81] Emetinæ et Bismuthi Iodidum (B.P.)

*Dose*.—1 to 3 grains (0.06 to 0.2 g.) (= approximately 1 gr. of emetine, or about 60 gr. of ipecacuanha) constitutes the average



daily dose, given in cachets, tablets, pills or capsules on an empty stomach last thing at night. Twelve doses are given in succession to make up the course. A total of 60 to 70 gr. (4 to 4.6 g.) may be necessary in some cases. If nausea and vomiting are produced, a sedative such as phenobarbitone  $\frac{1}{2}$  to 1 gr., or tincture of opium 10 to 20 m., should be given previously.

A brick-red powder containing 25 to 28% of emetine and 18 to 21% of Bi (1 g. of emetine and bismuth iodide is equivalent to approximately 0.4 g. of emetine hydrochloride).

**Manufacture.** Dissolve emetine hydrochloride 660 g. in water 32,000 ml. and treat with excess of the following solution:—Bismuth carbonate 290 g., potassium iodide 920 g., hydrochloric acid 900 ml, or q.s. to clear, and water 16,000 ml. Collect the precipitate, wash, and dry at 40°.

**Soluble** in acetone, insoluble in water and alcohol. In contact with dilute acids it is slightly decomposed but not dissolved. Is dissolved with decomposition in alkalis and strong acids.

**Uses.** Introduced in the belief that it would not be acted on by the stomach and that the emetine would be liberated in the intestine. Is considered effective in the treatment of chronic cases and of carriers. Its administration is sometimes combined with the injection of emetine hypodermically.

A Medical Research Committee reported that it cured the majority of carriers. Large quantities are essential—not less than 30 to 40 gr. in daily doses of 3 to 4 gr.

Emetine and bismuth iodide is of value in early stages and is capable of curing about 50% at that period, but when the disease becomes chronic it has proved a failure. Emetine alone in the acute phase is better, followed by emetine and bismuth iodide later. Risk of irritating action of emetine and bismuth iodide on the acutely inflamed bowel leading to serious intestinal hæmorrhage if used earlier.—P. H. Manson-Bahr, *Brit. med. J.*, ii/1921, 1115

A good deal of the disrepute into which emetine and bismuth iodide has fallen may be due to the fact that we focus our attention on the one relapsing case that does resist all forms of treatment, and forget the 99 that go their way rejoicing. Chenopodium oil should be tried in cases resisting emetine treatment.—G. W. Goodhart, *Lancet*, i/1923, 157

Vomiting, if delayed four hours after taking E.B.I., does not mean that it will not be absorbed. It appears to indicate that it is beginning to take effect.—P. Manson Rennie, *Lancet*, ii/1922, 1374

[P181] **Emetine Periodidum.** Syn. "E.P.I."

$C_{20}H_{40}O_4N_2I_8 = 1241.9$ .

**Dose.**—The average dose is 2 grains (0.12 g.) thrice daily for 15 days in capsules. Doses as high as 5 grains of the periodide, i.e.,  $1\frac{1}{2}$  grains of emetine, have been given.

A dark purple crystalline powder containing about 38.7% of emetine and 61.3% of iodine. It is obtained by precipitation of an emetine salt with a solution of iodine.

**Soluble** readily in acetone, slightly soluble in alcohol and chloroform, insoluble in water. Practically insoluble in dilute acids.

**Uses.** Is given in amœbic dysentery and is not acted on in the stomach. It causes less vomiting and nausea than emetine and

**bismuth iodide** It is also valuable in schistosomiasis, and for other indications for treatment with emetine

**AMŒBIC DYSENTERY** Emetine periodide 2 gr thrice daily for 15 days in capsule, ox bile 5 gr. being given in capsules simultaneously together with emetine hydrochloride 1 gr hypodermically or emetine in oil *per rectum* daily alternately for 6 days Treatment successful in highly resistant cases —J Graham Willmore and W. H. Martindale, *Trans R Soc trop Med (Hyg)*, 1923, 17, 13.

**SCHISTOSOMIASIS** The oral use clears up the urine of children intensely infected with *S. hæmatobium* as quickly and with almost as great certainty as emetine hydrochloride subcutaneously, and without risk 1 grain of the periodide thrice daily for 15 days was given —R M Gordon, *Brit med. J. Epit*, u/1926, 76

For tropical use, it is suggested, a preparation of emetine periodide in dried milk (1 grain in 2 drachms, i.e., 8 g) will be of value *Directions*—Two heaped teaspoonfuls in 3 ounces ( $\frac{1}{2}$  cupful) of warm water The majority of the children apparently successfully treated in 1926 were found to be passing live ova in 1930, but owing to the high degree of infection in the district it was impossible to say whether these were cases of relapse or reinfection.—R. M. Gordon and E. P. Hicks, *Ann trop Med Parasit*, Oct 22, 1930

Relatively safe, but may cause vomiting unless patients are kept in bed on strict diet Bilharzia infection often tends to die out of itself, and it seems desirable not to treat very young children exposed to further infection until a less toxic and more effective means of cure is available —F. G. Cawston, *Brit med J*, 1/1929, 890

[P181] **Auremetine** (Martindale, London). A combination of the periodides of emetine and auramine, containing 28% of emetine, 16% of auramine and 56% of iodine, for the treatment of amœbic dysentery It occurs as a maroon-coloured insoluble powder. Does not cause nausea, vomiting or purging. It is administered in capsules containing 1 gr, 4 times daily for 10 or 15 days, and the administration may be combined with that of acetarsol and bismuth subnitrate as for emetine hydrochloride

92% of cases treated by the method "responded," i.e., the patient regained his health, lost all clinical signs and symptoms of his disease (including sigmoidoscopic findings), his stools were negative on repeated examination It is impossible to guarantee permanent cure of chronic amœbic dysentery Auremetine has given some gratifying and more hopeful immediate results than any other essayed —J. Graham Willmore, *Proc R Soc Med.*, Nov, 1928

Combined treatment with Auremetine, bismuth, and acetarsol, has stood the hardest tests and stands first in general usefulness among all the remedies at hand, being the least toxic and the most widely applicable of them all —Otto Wilner, *J trop Med (Hyg.)*, 1928, 207

**SCHISTOSOMIASIS** in a child of 16 successfully treated with Auremetine Live ova disappeared from urine in 24 days Total dose 47 grains No vomiting or ill-effects —R M Gordon and E. P. Hicks, *Ann trop. Med. (Hyg)*, Oct. 22, 1930

**Cephaeline.**  $C_{28}H_{38}O_4N_2 = 466.3$ .

*Dose.*— $\frac{1}{12}$  to  $\frac{1}{4}$  grain (0.005 to 0.01 g.).

White silky needles becoming yellow on exposure to light

**Soluble** in alcohol, chloroform, benzene, caustic alkali solutions Is a more powerful emetic than emetine Its action is exerted slowly, and it should be given orally

By methylation it is converted into emetine

**Cephaeline Hydrochloride.**  $C_{28}H_{38}O_4N_2 \cdot 2HCl = 539.2$ .

*Dose.*—As for the base. Has been given as an emetic.

**Sedatussin** (Lilly, London). Cephaeline hydrochloride  $\frac{1}{4}$  gr., sodium benzoate 4 gr., tincture of sanguinaria 40 m., syrup of squill 48 m., svrup of tolu 60 m., menthol q s. Cough syrup.

**Gavano**, a German derivative of ipecacuanha, said to be a monomethyl ester of cephaeline in combination with an organic acid. Has been tried in intestinal amebiasis—less efficient but less toxic than emetine.—R. N. Chopra *et al*, *Indian med. Gaz.*, 1934, 130.

**Acalypha** (*B.P.C.*). *Syn.* INDIAN ACALYPHA, MUKTA-JHURI. The fresh or dried entire plant, *Acalypha indica* (Euphorbiaceæ). A gastro-intestinal irritant. Has been used as a substitute for ipecacuanha.

**Adhatoda** (*B.P.C.*). *Syn.* MALABAR NUT LEAVES, VASAKA. The leaves of *Adhatoda Vasica* (Acanthaceæ). Used as an expectorant in the form of liquid extract, syrup, or tincture, also smoked for asthma.

**Angelica Radix** (*B.P.C.*).

*Dose.*—10 to 30 grains (0.6 to 2 g.).

The dried rhizome and roots of *Angelica Archangelica* (Umbelliferae). Contains 0.3 to 1% of volatile oil. The powder and an infusion (1 in 20) have been administered for their stimulant, diaphoretic and expectorant properties. The seeds (*Angelica Fructus B.P.C.*) have similar properties.

**Calotropis** (*B.P.C.*). *Syn.* MUDAR. *Dose.*—Expectorant, 3 to 10 grains (0.2 to 0.6 g.); emetic,  $\frac{1}{4}$  to 1 drachm (2 to 4 g.). Dried root-bark of *C. procera* and *C. gigantea* (Asclepiadaceæ). Used in the East instead of ipecacuanha. *Tinctura Calotropis*, *dose.*— $\frac{1}{4}$  to 1 drachm, 1 in 10.

**Eriodictyon** (*B.P.C.*). *Syn.* YERBA SANTA

*Dose.*— $\frac{1}{4}$  to 1 drachm (1 to 4 g.). The dried leaves of *Eriodictyon glutinosum* (Hydrophyllaceæ). Stimulant in bronchitis, phthisis and other catarrhal affections. Is administered as a liquid extract, 1 in 1, prepared with alcohol 25%, *dose*—15 minims. The liquid extract greatly reduces the bitterness of mixtures containing quinine or other bitter drugs.

*Eriodictyon* (*U.S.P. XI*) is from *E. Californicum*.

**Fluidextractum Eriodictyi** (*U.S.P. XI*). *Average dose.*—15 minims (1 ml.). 1 in 1, prepared with a mixture of alcohol 95% 4 parts and water 1 part.

The action of liquid extract of eriodictyon in removing the bitter taste of solutions of quinine or strychnine is due to the presence of resinous matter which adsorbs the alkaloid.—Fantus, Dyniewicz and Dyniewicz, *J. Amer. pharm. Ass.*, 1933, 323.

**Grindelia** (*B.P.C.*).

The dried leaves and flowering tops of the "Gum Plant," *Grindelia camporum* (Compositæ). The involucre, and often the leaves, are coated with resin, 20% or more, to which the medicinal action is due.

*Uses.* For the spasmodic attacks which occur in asthma, whooping-cough and bronchitis, and given in heart disease to slow and regulate the pulse.

**Extractum Grindeliæ Liquidum** (*B.P.C.*) 1 in 1.

*Dose.*—10 to 20 minims (0.6 to 1.2 ml.) at the onset of a paroxysm of asthma, repeated every hour, in sweetened water or milk.

A 1 in 10 dilution has been used in dermatitis due to the poison ivy, *Rhus toxicodendron*.

**Extractum Grindeliæ.**

*Dose.*—2 to 3 grains (0.12 to 0.2 g.) 3 times a day.

Prepared by evaporating the alcoholic percolate.

[P1-81] **Extractum Grindeliæ Compositum.**

*Dose.*—1 drachm (4 ml.) with a small quantity of spirit, *e.g.*, 2 drachms of brandy in  $\frac{1}{4}$  tumbler of hot water.

Liquid extracts of grindelia, chekan and eriodictyon each 1, liquid extract of quebracho 3. Suggested for use in asthma.

[P1] **Grindeline** (*Oppenheimer, London*) Dose —1 to 2 drachms in water every 2 to 4 hours. Containing liquid extract of grindelia 15 m, potassium iodide 2 gr, glyceryl trinitrate  $\frac{3}{16}$  gr., tincture of euphorbia pilulifera 20 m in each drachm.

[P1] **Mist. Grindeliæ** (*N.I.F.*). Liquid extract of grindelia 10 m, ethereal tincture of lobelia  $7\frac{1}{2}$  m, tincture of belladonna 5 m, liquid extract of liquorice 10 m, mucilage of acacia 30 m, chloroform water to  $\frac{1}{2}$  oz.

[P1] **Spiritus Grindeliæ Compositus.**

Dose —1 to 2 drachms (4 to 8 ml) in water every 2 to 4 hours while attack of asthma lasts

Liquid extract of grindelia 15 m, sodium iodide 2 gr., solution of glyceryl trinitrate  $\frac{1}{2}$  m, tincture of euphorbia pilulifera 20 m., spirit of chloroform to 1 drachm.

**Holarrhena** (*B.P.C.*). *Syn* CONESSI BARK, TELICHERRY BARK, KURCHI OR COORCHI. The bark of the stem and root of *H. antidysenterica* (*Apocynaceæ*), a small deciduous tree found throughout India. The plant, as also *H. Congolensis* from the Congo, contains conessine,  $C_{12}H_{20}N$ . This alkaloid has strong inhibitory action on amœbæ—equal to that of emetine. It is 50% less toxic than the latter. Conessine salts can be given *per os* and intravenously, but subcutaneously they produce necrosis at site of injection. The bark has remarkable effect in amœbic dysentery. Suggested dose of powdered bark 2 to 5 grains. A liquid extract 1 = 1 has been used with good result in daily doses of 6 to 8 drachms. Kurchi tablets are made 5 grains.

Antidysenteric value compares favourably with any other remedy in vogue and depends on use of entire seed or bark. Recommended daily dose of 60 to 120 grains of powdered bark in 3 or 4 portions—*Lancet*, 1/1928, 39; see also T A Henry and H C Brown, *ibid*, 108

**AMœBIC DYSENTERY** Comparative treatment of 154 cases with Alcresta Ipecac, emetine injections, emetine injections plus bismuth *per os*, emetine and bismuth iodide, Yatren, Stovarsol and kurchi bark, showed that the last two gave the best results, the ratio of probable cures to failures in each of these cases being 1·1·1—R Knowles, *per Lancet*, 11/1928, 714. Total kurchi bark alkaloids used with success in amœbiasis—2 grain doses intramuscularly or liquid extract orally—*Per Med. Annu*, 1931, 17

**Kurchi Bismuth Iodide.** Dose —4 grains twice daily for 10 days in amœbiasis. In acute amœbic infections nine  $\frac{1}{2}$ - to 1-grain doses of the total kurchi bark advised—H W Acton and N. R. Chopra, *Med. Annu*, 1931, 17.

*Holarrhena* var also contain the alkaloid holarrhenine.

Intramuscular injections of 2 gr. of kurchi alkaloid as effective as emetine, but painful. Kurchi-bismuth-iodide compares favourably with corresponding emetine compound in 10 gr doses twice daily, preceded half an hour beforehand by 60 gr. of sodium bicarbonate and 40 gr of sodium citrate, for 10 days or longer. Second course not recommended—H W. Acton and R N. Chopra, *Indian med Gaz.*, 1932, 6

**Phytolacca** (*B.P.C.*). *Syn* POKE ROOT

Dose.—1 to 5 grains (0·06 to 0·3 g.).

The root of *Phytolacca decandra* (*Phytolaccaceæ*) containing a bitter resin. Is emetic, purgative and mildly sternutatory. Has been given in chronic rheumatism, and used as a local application in mammitis and mumps.

Phytolaccin, dose—1 to 5 grains, is the dried extractive.

**Antidotes.** Empty stomach by emetic or stomach tube. Give stimulants, *e.g.*, aromatic spirit of ammonia,  $\frac{1}{2}$  dr. in water. Digitalis may be necessary, and morphine,  $\frac{1}{2}$  gr hypodermically, for pain.

**Sanguinaria (B.P.C.).** *Syn.* BLOOD ROOT. *Dose.*—1 to 5 grains (0.06 to 0.3 g.). The dried rhizome of *S. Canadensis* (Papaveraceæ). Expectorant in chronic bronchitis. Has been given as a 10% tincture, *dose.*—15 minims. A resinoid extractive, sanguinarin, *dose*— $\frac{1}{4}$  to 1 grain, is made.

**Simaruba (B.P.C.).** *Dose.*— $\frac{1}{4}$  to  $\frac{1}{2}$  drachm (1 to 2 g.). The dried root-bark of *S. amara* (Simarubaceæ). Used as a bitter, and as an astringent in dysentery. Administered as a decoction (1 in 20).

**Decoctum Simarubæ et Punice Granati.** Add simaruba bark, pomegranate fruit rind and gum arabic of each 15 g. to a litre of water, and boil down to  $\frac{1}{2}$  litre. *Dose*—30 ml 3 or 4 times daily. Cures dysentery rapidly (Egypt).—Ph Notes. The quantities and the ingredients have been varied from time to time. The Ministry of Health replaced cinnamon for the acacia.—*Chem & Drugg*, 1920, 1320. See also *ibid*, 1/1921, 442.

## JALAPA

(with IPOMŒA etc.)

*B.P., P. Helv. V, P. Dan.*

*Syn.* BRYONE NOIRE OR MECCHOACAN NOIR.

The dried tubercles of *Ipomœa purga* (Convolvulaceæ). A powerful purgative producing watery stools, it is apt to gripe, and must be avoided if the bowels are inflamed. Used to reduce dropsy of Bright's disease, and to relieve uræmia. When Jalapa is prescribed Jalapa Pulverata is to be dispensed.

**Jalapa Pulverata (B.P.).**

*Dose*—5 to 20 grains (0.3 to 1.2 g.).

Jalap in fine powder adjusted with exhausted jalap or lactose to contain 10% of resin.

**Pulvis Jalapæ Compositus (B.P.).**

*Dose*—10 to 60 grains (0.6 to 4 g.).

Powdered jalap 30% with ginger 10% and potassium acid tartrate.

**Tinctura Jalapæ (B.P.C.)**

*Dose*— $\frac{1}{2}$  to 1 drachm (2 to 4 ml). Contains 1.5% of resin.

**Tinctura Jalapæ Composita (B.P.C.)**

*Dose.*— $\frac{1}{2}$  to 1 drachm (2 to 4 ml) Contains 1 in 12 $\frac{1}{2}$  of jalap with scammony resin and turpeth.

**Jalapæ Resina (B.P.C., P.G. VI, P. Ital. V, F.E. VIII, P. Belg. IV, P. Helv. V and P. Dan.).**

*Dose.*—1 to 5 grains (0.06 to 0.3 g.).

Contains two glucosidal resins, about 90% convolvulin (*syn.* JALAPURGIN), soluble in alcohol, but insoluble in ether, together with about 10% soluble in ether and in alcohol. The latter, orizabin or jalapin (Mayer), the principal constituent of spurious jalap (*Ipomœa simulans* and *I. orizabensis*), is identical with scammonin from scammony root. It is cheaper and less active. B.P.C. requires not less than 85% of ether-insoluble resins.

A jalap resin, known as *Regina de Batata de Purga*, and extracted from the tubercle of *Convolvulus Operculatus*, is extensively used in Brazil. It possesses the same properties as the official jalap, but is practically devoid of any subsequent constipating action. *Dose*—0.25 to 2 g.—*Chem & Drugg*, 1/1925, 854.

**Jalapinum (B.P.C.).**

*Dose.*—1 to 5 grains (0.06 to 0.3 g.).

The ether-insoluble portion of the resin obtained from jalap, occurring as a white odourless powder with acrid taste, m.p. about 155°. **Soluble** in alcohol, glacial acetic acid and ethyl acetate, insoluble in ether and water, slightly soluble in chloroform. Is considered less active than jalap resin.

It should be distinguished from the substance known in Germany as jalapin, which is the ether-soluble portion of jalap resin.

**Ipomœa (B.P.).** *Syn.* ORIZABA JALAP ROOT, MEXICAN SCAMMONY ROOT.

*Dose.*—5 to 20 grains (0.3 to 1.2 g.).

The dried root of *I. orizabensis* (Convolvulaceæ).

**Scammonia Resina (B.P.).** *Syn.* RESINA IPOMŒÆ (U.S.P. X)

*Dose.*— $\frac{1}{2}$  to 3 grains (0.03 to 0.2 g.).

**Soluble** in alcohol 90%, insoluble in water, wholly or partly soluble in ether.

**Pulvis Scammonia Compositus (B.P.C.)**

*Dose.*—10 to 20 grains (0.6 to 1.2 g.) Scammony resin 50% with jalap and ginger.

**Pilula Scammonia Composita (B.P.C.).**

*Dose.*—1 or 2 pills. Contain 1 gr. each of scammony resin, jalap resin and curd soap, and  $\frac{1}{2}$  gr. of ginger.

**Scammonin** is the ether-soluble portion of scammony resin. Purgative in obstinate constipation, producing copious watery evacuation in a few hours. Does not act until reaching the duodenum.

**Scammonium (B.P.C.),** *syn.* VIRGIN SCAMMONY, *dose*—5 to 10 grains (0.3 to 0.6 g.), is the gum-resin obtained from scammony root. It occurs in blackish pieces giving an emulsion with water. It resembles scammony resin in its action.

**Cambogia (B.P.C., P. Helv. V, P. Austr., Fr. Cx.).** *Syn.* GOMME GUTTE

*Dose.*— $\frac{1}{2}$  to 2 grains (0.03 to 0.12 g.). *P. Helv. V* max. single dose 3 grains approx., max. in 24 hours 10 grains. Yellow gum-resin from *Garcinia Hanburyi* (Guttiferæ) growing in Siam. A powerful purgative, and may cause severe griping. Will expel tapeworm. Is rarely now given alone. Indian gamboge, from *G. Morella*, is similar.

**Kaladana (B.P.C.)** *Syn.* PHARBITIS SEEDS

*Dose.*—30 to 45 grains (2 to 3 g.). The dried seeds of *Ipomœa hederacea* (Convolvulaceæ). Purgative and anthelmintic.

**Pulvis Kaladana Compositus** and **Tinctura Kaladana** are prepared in the same way as the corresponding preparations of jalap, and are used instead of them in India and the East.

**Kaladana Resina.** *Dose.*—2 to 8 grains (0.12 to 0.5 g.).

Useful hydragogue, used as a substitute for jalap resin in India and the East.

**Leptandra (B.P.C.).** *Syn.* BLACK ROOT, CULVERS ROOT.

*Dose.*— $\frac{1}{2}$  to 1 drachm (1 to 4 g.).

The dried rhizome and roots of *Veronica virginica* (Scrophulariaceæ). Cholagogue, reputed to act without irritating the bowels. Often combined with podophyllin or euonymin.

**Extractum Leptandræ** (B.P.C.). *Syn.* LEPTANDRIN.

*Dose.*— $\frac{1}{2}$  to 2 grains (0.03 to 0.12 g.). A dry extract.

[P1] **Tabellæ Leptandræ Compositæ** (B.P.C.). *Syn.* TABELLÆ LAXATIVÆ COMPOSITÆ, VEGETABLE LAXATIVE TABLETS. *Dose.*—1 to 3 tablets.

Contain compound extract of colocynth 1 gr.,  $\frac{1}{2}$  gr. each of leptandra, jalap resin, resin of podophyllum, dry extract of hyoscyamus and extract of taraxacum, and oil of peppermint.

**Turpethum** (B.P.C.). *Syn.* INDIAN JALAP. *Dose.*—5 to 20 grains (0.3 to 1.2 g.). The dried root and stem of *Ipomœa Turpethum* (Convolvulacæ). Contains 5 to 10% of resin and is used in the East in place of jalap.

## KRAMERIA

(with KINO, CATECHU, etc.)

*B.P., P. Helv. V, P. Dan.*

*Syn.* RHATANY ROOT.

The dried root of *Krameria triandra* (Polygalacæ). Contains about 8% of a tannin. Astringent in relaxed throat. Also used in tooth powders when gums are liable to bleed, and in mouth-washes, also for bleeding from nose and bowels, and for diarrhœa.

**Extractum Krameriz Siccum** (B.P.).

*Dose.*—5 to 15 grains (0.3 to 1 g.). The aqueous percolate evaporated to dryness under reduced pressure.

**Infusum Krameriz Concentratum** (B.P.C.).

*Dose.*— $\frac{1}{2}$  to 1 drachm (2 to 4 ml.). 1 in 2 $\frac{1}{2}$ .

**Infusum Krameriz Recens** (B.P.C.) *Syn.* INFUSION OF RHATANY.

*Dose.*— $\frac{1}{2}$  to 1 ounce (15 to 30 ml.). 1 in 20.

**Tinctura Krameriz** (B.P.).

*Dose.*— $\frac{1}{2}$  to 1 drachm (2 to 4 ml.). 1 in 5 of 60% alcohol by percolation

**Trochiscus Krameriz** (B.P.) contains 1 gr. of the dry extract.

[D-P1 81] **Trochiscus Krameriz et Cocainæ** (B.P.) contains 1 gr. of the dry extract with  $\frac{1}{10}$  gr. of cocaine hydrochloride

**Kino** (B.P.C., U.S.P. XI, P. Helv. V).

*Dose.*—5 to 20 grains (0.3 to 1.2 g.). U.S.P. XI average dose 8 grains.

The dried juice from the trunk of *Pterocarpus Marsupium* (Leguminosæ). Partly soluble in cold water, more soluble in hot water and alcohol 90%, nearly insoluble in ether. Contains 70 to 80% of kinotannic acid. Astringent for diarrhœa, and as Trochisci for relaxed condition of the throat. The powder is also insufflated to check epistaxis.

**[P1-81] Pulvis Kino Compositus (B.P.C.).**

*Dose.*—5 to 20 grains (0.3 to 1.2 g.).

Kino 75%, powdered opium 5%, and cinnamon 20% (*exempt*(D)).

**Tinctura Kino (B.P.C.).**

*Dose.*— $\frac{1}{2}$  to 1 drachm (2 to 4 ml.). 1 in 10.

The tincture may gelatinise, due to enzymes, on storage.

**Incompatible** with mineral acids and alkalis and with substances precipitable by the tannin it contains.

**Tinctura Kino (U.S.P. XI).** *Average dose*—30 minims (2 ml.).

1 in 5; double the strength of the U.S.P. X tincture.

**Kino Eucalypti (B.P.C.). Syn. RED GUM, GUMMI EUCALYPTI.**

*Dose.*—5 to 20 grains (0.3 to 1.2 g.).

An exudation from *Eucalyptus rostrata* (Myrtaceæ), and other species. About 80% of it is soluble in cold water, and about 90% in alcohol 90%. Used in diarrhœa, and relaxed throats, and as astringent in dentistry, cuts, etc. As astringent in hæmorrhage and in relaxed conditions of the larynx and trachea, it is used mixed with an equal weight of starch. As a suppository, 5 gr. in oil of theobroma may be used.

To be distinguished from the common Australian or Botany Bay kino, said to be from *E. resinifera*.

**Decoctum Kino Eucalypti.** *Dose.*—2 to 4 drachms. 1 in 40; boil and strain. Used as a gargle and for diarrhœa.

**Extractum Kino Eucalypti Liquidum (B.P.C.). Syn. EXTRACTUM GUMMI RUBRUM LIQUIDI.**

*Dose.*— $\frac{1}{2}$  to 1 drachm (2 to 4 ml.). 1 in 4.

**Gargarisma Kino Eucalypti (B.P.C.)** Liquid extract of kino eucalyptus 6 25% v/v.

**Tinctura Kino Eucalypti (B.P.C.). Syn. TINCTURA GUMMI RUBRA**

*Dose*—15 to 40 minims (1 to 2.6 ml.). 1 in 4

**Trochisci Kino Eucalypti (B.P.C.) Syn. RED GUM LOZENGES, EUCALYPTUS GUM LOZENGES** Contain 1 grain

**Trochisci Eucalypti Compositi.**

Potassium chlorate 2 gr., powdered cubeb  $\frac{1}{2}$  gr., eucalyptus gum 1 gr. with fruit paste. Useful in congested and relaxed throats, especially when mucus secretion is arrested.

**Bela (B.P.C.) Syn. Bael Fruit.** The fresh or dried half-ripe fruit of *Aegle Marmelos* (Rutaceæ). Mild astringent. The fresh fruit is useful in dysentery and in dyspepsia.

**Extractum Belæ Liquidum (B.P.C.).** *Dose.*—1 to 2 drachms (4 to 8 ml.). 1 in 1.

**Buteæ Gummi (B.P.C.). Syn. BENGAL KINO.** Obtained from incisions in the stem of *Butea frondosa* (Leguminosæ). Used in the East in place of kino.

**Catechu (B.P., P. Helv. V). Syn. CATECHU PALLIDUM, GAMBIR.**

*Dose.*—5 to 15 grains (0.3 to 1 g.).

A dried aqueous extract of the leaves and young shoots of *Uncaria gambier* (Rubiaceæ). Soluble in water to the extent of about 50%. Astringent in diarrhœa.

**Mist. Catechu Co. (N.I.F.).** Powdered catechu 10 gr., aromatic powder of chalk 15 gr., chalk 15 gr., chloroform water to  $\frac{1}{2}$  oz.

**Pulvis Catechu Compositus (B.P.C.).** *Dose*—10 to 60 grains (0.6 to 4 g.). 1 in 2 $\frac{1}{2}$ , with kino, kramena, cinnamon and nutmeg



**Tinctura Catechu (B.P.).** *Dose.*— $\frac{1}{2}$  to 1 drachm (2 to 4 ml.).

1 in 5 of alcohol 45% with cinnamon 1 in 20.

**Trochiscus Catechu (B.P.C.)** contains 1 grain. For relaxed throat

**Catechu Nigrum (B.P.C.).** *Syn.* CUTCH.

*Dose.*—5 to 15 grains (0.3 to 1 g.)

An extract prepared from the heartwood of *Acacia Catechu* (Leguminosæ) used for the same purposes as catechu

**Rhus (B.P.C.).** *Syn.* RHUS FRUCTUS, SUMACH, SUMAC BERRIES

*Dose.*—10 to 30 grains (0.6 to 2 g.).

The dried fruits of *R. Glabra* (Anacardiaceæ). Astringent and reputed diuretic. The liquid extract (1 in 1) and decoction (1 in 20) have been used in gargles.

**Rhus Aromatica** (Anacardiaceæ) (Sweet or Fragrant Sumach) The bark of this Canadian and U.S. plant contains tannin and volatile oils *Dose*—5 to 30 grains has given results in incontinence of urine

**Rhus Toxicodendron** (Anacardiaceæ). *Syn.* POISON OAK, POISON IVY LEAVES. *Tincture.* *Dose.*—2 to 15 minims Imported from North America, prepared from fresh leaves 1, alcohol 2 Used for rheumatism in chronic skin affections, paraplegia, and incontinence of urine from atony of the bladder. Also for hæmorrhoids. Whitla says it gives satisfaction, but may irritate stomach and bowels. The poisoning by the "Toxicodendrol" contained, takes the form of an itching, burning, erythematous and herpetiform rash.

Swab skin with 5% potassium permanganate—recovery rapid A 5% ferric chloride solution in 50% glycerin, washed freely on skin will act as preventive of dermatitis.—*Amer. J. Pharm.*, June, 1928, 416

**Coto (B.P.C.).** *Syn.* PARACOTO.

*Dose.*—1 to 8 grains (0.06 to 0.5 g.), in powder, 4 to 6 times a day

A bark of unknown botanical origin imported from Bolivia, probably from a species of *Nectandra*.

*Botanical source* of coto bark given as *Nectandra Coto* by Dr. Rusby. It seems probable that like the cinchona genus there may be several allied species—E. M. Holmes, *Pharm. J.*, 1/1923, 240

**Incompatible** with Mistura Creta

*Uses.* For cholera, and especially the diarrhœa of phthisis, for night sweats, and for gout and rheumatism It is rich in resins, which give it a pungent taste

**Extractum Coto Liquidum (B.P.C.).** 1 = 1 of bark

*Dose.*—5 to 15 minims (0.2 to 1 ml.)

**Tinctura Coto (B.P.C.)** *Dose*—10 to 30 minims (0.6 to 2 ml.) 1 in 10

**Mistura Anti-choleraica** (Royal Coll. Phys., Form II)

Aromatic sulphuric acid 15 minims, compound tincture of camphor 30 minims, compound tincture of chloroform, tincture of coto, of each 20 minims, syrup of orange flower 1 drachm, peppermint water to 1 ounce *Dose.*—1 ounce every 3 or 4 hours. This preparation has been found invaluable

Form I will be found in the Xth Edition, p. 105 For further anti-cholera mixtures see Opium.

**Cotoin.** *Dose*— $\frac{1}{2}$  to 2 grains (0.03 to 0.12 g.) every 2 or 3 hours in pill or diluted mucilage 4 grains have been used in dysentery

A bitter principle in yellow crystalline powder, slightly soluble in water, soluble in alcohol. Melting point 130°. The dust is irritating to the nostrils.

**Rosæ Petalum (B.P.C.).** *Syn.* RED-ROSE PETALS. The petals of the red or French rose, *Rosa gallica*. *Flos Rosæ* (P. Helv. V) is from *R. gallica* or *R. centifolia*.

**Confectio Rosæ Gallicæ (B.P.C.), syn.** CONFECTION OF ROSES, consists of the fresh petals beaten to a paste with sucrose.

**Infusum Rosæ Acidum Concentratum (B.P.C.)**

*Dose.*— $\frac{1}{2}$  to 1 drachm (2 to 4 ml.)

About 1 in 5. Approximately 8 times the strength of the fresh infusion.

**Infusum Rosæ Acidum Recens (B.P.C.).**

*Dose.*— $\frac{1}{2}$  to 1 ounce (15 to 30 ml.). 1 in 40, with 1 in 80 of dilute sulphuric acid.

**Syrupus Rosæ (B.P.C.).**

**Dose**— $\frac{1}{2}$  to 1 drachm (2 to 4 ml). A solution of sucrose in an acidified aqueous infusion of the petals.

**Rosæ Centifoliæ Petalum**, *syn* PALE-ROSE PFTAI, is obtained from the cabbage or Provence rose, *Rosa centifolia*

**Rosæ Fructus (B.P.C.).** *Syn* HIPS The fresh ripe fruits of the dog rose, *Rosa canina* (Rosaceæ) and other closely allied species

**Confectio Rosæ Caninæ (B.P.C.),** *syn*. CONFECTION OF HIPS, consists of the hips deprived of their achenes and beaten to a pulp with sucrose Occasionally used as a pill excipient.

**Salix (B.P.C.).** *Syn* WILLOW BARK. The bark of *S. alba* and other species Contains tannin and salicin.

**Extractum Salicis Nigræ Liquidum (B.P.C.)** **Dose.**— $\frac{1}{2}$  to 1 drachm (1 to 4 ml). 1 in 1.

## LAMELLÆ

Ophthalmic lamellæ or discs are prepared with gelatin, glycerin and water The discs are  $\frac{1}{8}$  inch (3.175 mm.) in diameter. Directions for making them are given in the B.P.

[P 181] **Lamella Atropinæ (B.P.)** weighs  $\frac{1}{10}$  gr. and contains  $\frac{1}{1000}$  gr. of atropine sulphate.

Also prepared containing  $\frac{1}{1000}$  and  $\frac{1}{100}$  gr.

[D P 181] **Lamella Cocainæ (B.P.)** weighs  $\frac{1}{10}$  gr. and contains  $\frac{1}{10}$  gr. of cocaine hydrochloride.

[P 181] **Lamella Homatropinæ (B.P.)** weighs  $\frac{1}{10}$  gr. and contains  $\frac{1}{1000}$  gr. of homatropine hydrobromide

[P 181] **Lamella Physostigminæ (B.P.).** *Syn.* LAMELLA OF ESERINE. Each weighs  $\frac{1}{10}$  gr. and contains  $\frac{1}{1000}$  gr. of physostigmine salicylate.

## LIGATURES AND SUTURES

Surgical ligatures and sutures may be of two types, those which are absorbed by the body and disappear from the wound, and those which are not absorbed. The absorbable type includes catgut, kangaroo tendon and strips of skin, whilst the non-absorbable includes silkworm gut, silk, horsehair and Japanese synthetic gut.

*The Therapeutic Substances Act, 1925 (Regulations, 1931) controls the manufacture and importation for sale of any ligature or form of binding material prepared from the gut or any tissue of an animal and offered for sale as sterile and ready for use in surgical operations on the human body.*

These regulations apply to sterilised catgut and sterilised kangaroo tendon (but not to horsehair or silkworm gut), and their manufacture can only be carried out under licence from the Ministry of Health. The control exercised under the Act has raised very considerably the standard of sterility of such ligatures on sale in this country.

**Catgut** is prepared from the small intestine of young lambs, and consists of the *submucosa* only, the other layers being scraped away during the course of manufacture. The raw material for

catgut manufacture is heavily infected with a variety of micro-organisms, among which there may occur pathogenic anærobcs, so that sterilisation becomes a matter of great importance.

The intestines, after removal, are stroked free from fæces and immediately salted or frozen. In the factory the blocks of frozen gut are thawed out, thoroughly washed, soaked in weak alkali to make them soft and supple and then split longitudinally into ribbons. They are next well scraped to free them from the unwanted layers, leaving the submucosa only, and passed through a disinfectant solution as a preliminary sterilisation process. A certain number of ribbons, according to the gauge of catgut desired, is spun or twisted under tension into a single strand. The strands are then dried under tension on frames. This produces "raw catgut" and, if a disinfecting solution has been used, "raw 'internally sterilised' or 'partially sterilised' catgut." This so-called internally sterilised catgut is not necessarily sterile internally, as the Therapeutic Substances Act does not control this stage of its manufacture. Unfortunately, purchasers of it are apt to assume that the product requires less sterilisation than "raw catgut," and this assumption has undoubtedly led to wound infection following the use of such catgut, sterilised in hospitals for their own use.

The dried raw catgut is polished by means of emery paper or pumice stone and then graded according to thickness. Sterilised surgical catgut is supplied by manufacturers in different gauges, which are classified 000000, 00000, 0000, 000, 00, 0, 1, 2, 3, 4, 5 and 6. The first is extremely fine and No. 6 very stout. The sizes in common use range from 00 to 3. There are, however, no standard gauges, so that the No. 0 gut, for instance, of one manufacturer is not necessarily of exactly the same calibre as the No. 0 gut of another maker.

In order to delay the absorption of catgut in the body, the raw catgut is treated with a variety of substances such as potassium dichromate or tannic acid. *Lister's sulphochrome catgut* is of this type, and is prepared by soaking raw catgut 24 hours in 20 times its weight of "preparing liquid"—made as follows:—Dissolve chromic acid 4, in water 240, add sulphurous acid *q.s.* to produce the green colour of chromium sulphate. Then add water to make 480 (weight), next add solution of mercuric chloride 2 in water 320. Dry the catgut under tension. Lister considered that such sulphochrome catgut does not begin to be absorbed for about 10 days, and is then gradually eroded, although it retains considerable firmness to the last.

Manufacturers supply so-called 10, 20, 30-day sterilised catguts indicating the time of durability in the body, but such times are probably unreliable and very approximate, since the rate of absorption of the ligature varies with the type of tissue in which it is embedded, and with the individual.

**Sterilised Catgut.** Owing to the nature of its origin, catgut must be suspect with regard to the possible presence of such

pathogenic organisms as those of tetanus and anthrax, and any process of sterilisation must be effective in killing spores of these organisms when they occur *embedded* in the strands due to the twisting of the ribbons. This constitutes the chief problem in the sterilisation process—to find the reagent which will penetrate the tissue without unduly altering the physical characters of the material. Surface sterilisation can easily be accomplished. Surgical catgut must be of good tensile strength, supple and sterile. The tensile strength should be good on the length and on the knots. The tensile strength may be lost during the washing and spinning process, and particularly during the sterilisation process.

Many reagents are used and have been suggested as sterilising agents, such as phenol in oil, mercuric chloride, mercuric biniodide, silver compounds, essential oils such as clove, juniper, turpentine, peppermint, lavender, cajuput and eucalyptus, formaldehyde, picric acid, hydrogen peroxide and iodine. The production of surgical catgut has been the subject of a report by the M.R.C. (W. Bullock, L. H. Lampett and J. H. Bushill, *Spec. Rep. Ser. med. Res. Coun., Lond.*, 1929, No. 138; *Brit. med. J.*, 11/1929, 918). In this report it is concluded that hydrogen peroxide and iodine are the most effective sterilising agents, and that iodine is the most practical. Iodine readily penetrates the collagen material of the catgut and effectively sterilises it. When iodine reacts with collagen, acid is produced, and as this will cause a loss of tensile strength it is advisable to have some potassium iodate present in the solution to prevent the development of acid. It is also usual to have a little glycerin present, as this gives suppleness to the gut and results in considerable increase in the strength on the knot, which is important. Ligatures which have been in contact with glycerin acquire a very soft, silky texture and are very suitable for the surgeon's use. An aqueous solution of the following composition is recommended as a sterilising solution. Iodine 1%, potassium iodide 2%, potassium iodate 0.25%, glycerin 5 to 10%. The raw catgut should be immersed whilst under tension in this solution for 8 to 9 days until it has absorbed 12% of its weight of iodine. This ensures sterility. The treated gut should then be freed from free iodine by immersion in several changes of 70% alcohol containing 2% of glycerin. It is important that such alcohol should be filtered through a bacterial filter before use, as commercial spirit (contrary to popular belief) is not necessarily sterile but often contains the spores of anaerobes. An iodine solution of this type is often used to produce the "internally sterilised" raw catgut.

#### METHODS OF STERILISATION.

**Heat.** Many manufacturers have their own secret processes of sterilisation and some are successful with a process of heat sterilisation. Sterilisation by heat alone must be carefully controlled, otherwise there may be imperfect sterilisation or, conversely, a big decrease in tensile strength. Heat sterilisation usually involves heating the catgut in such fluids as benzene, toluene or xylol, or heating in steam under pressure at a temperature of about 160°.

**Mercurial Solutions.** The M.R.C. report is severely critical of the use of mercuric biniodide as a sterilising agent for catgut. It is stated that there appears

to be a rooted belief among English and American catgut manufacturers that mercuric iodide possesses some valuable or mysterious property which improves the tensile strength of the finished ligatures. A large number of experiments prove this to be quite fallacious. A 1% aqueous solution of mercuric iodide in potassium iodide did not kill *B. mesentericus rubra* on silk threads in 3 years.

Mercuric chloride has been greatly overrated as a disinfectant, mostly as the result of employing inadequate tests for sterility of the finished gut. Both the above solutions, as far as catgut is concerned, are more bacteriostatic than bactericidal, although they may have some disinfectant action on the exterior of the catgut, and for this reason they are often employed for "filling solutions" (i.e., for filling the containers in which the catgut is offered for sale) even when another process has been used for the actual sterilisation of the gut.

**Hydrogen Peroxide** is a most efficient sterilising agent for catgut, but it has a swelling action upon spun gut. It is therefore never employed by itself, but is generally used for treating the wet gut as a preliminary to the action of iodine.

**Essential oils** have been largely used in hospitals for the sterilisation of catgut for their own use. They have, however, a negligible action on spore-bearing bacteria.

### TESTS FOR STERILITY.

It is very important, in assessing the value of any reagent as a sterilising agent for catgut, to ensure that any trace of it remaining in the ligature is entirely removed before testing the material for sterility. Otherwise such traces may act bacteriostatically in the culture medium and a false result be obtained. Neglect of this precaution has been the cause of reliance being placed on such disinfectants as mercuric chloride, mercuric biniodide, essential oils, etc., none of which has the power of penetrating catgut sufficiently to ensure internal sterilisation.

The test for sterility required by the Therapeutic Substances Act specifies that the sample taken for test shall be not less than 1% of the batch. After draining off the filling solution, the ligature is immersed in sterile distilled water and incubated at 37° for 24 hours, aseptic precautions being taken. The sample is then transferred aseptically to a sterile fluid containing substances which will have the effect of removing or destroying any traces of antiseptic left in the gut. The solution prescribed for this purpose in the regulations consists of a 1% sterile solution of sodium thiosulphate and sodium carbonate in distilled water. This is only suitable for removing iodine. If this method is not suitable for the particular antiseptic used, the licensee must seek the approval of the licensing authority for alternative methods. It is incubated in this fluid at 37° for 24 hours. The sample is then removed, well washed and one half placed in a culture medium suitable for aerobic organisms and the other half in a medium for anaerobic organisms. Incubation of the tests must be carried out at 37° for 12 days, and the cultures must be examined daily for the growth of bacteria.

The preparation of sterile catgut in hospitals for use in the operating theatre is not controlled by the Therapeutic Substances Act, but Sir W. Dalrymple-Champneys (*Proc. R. Soc. Med.*, 1936, 29, 465) appeals to hospitals to use only tested sterile catgut and thus eliminate the possibility of serious infection from its use.

It should be noted that the term "boilable catgut," which is occasionally used, has no significance, since catgut cannot be boiled.

### FILLING AND LABELLING.

After sterilisation the catgut is packed into glass tubes containing an antiseptic solution and sealed. Sterilised ligatures produced under licence must be labelled with the proper name of the substance, the licence number, the batch number, the name and address of the manufacturer of the final product, and the date of manufacture (i.e., the date on which the test for sterility was completed).

Recent references to the sterilisation of catgut.—

Clock, *Surg. Gynec. Obstet.*, 1933, 56, 149, 1934, 59, 899.

Mackie. "An inquiry into post-operative tetanus. A report to the Scottish Board of Health." London, 1928.

Mackie. Report to the Department of Health for Scotland, 1929.

*Memorandum on Catgut*, No. 199 Med., H.M.S.O.

*Pharm. J.*, 1/1936, 254

**Kangaroo tendon** consists of the tendons dissected out from kangaroo tails. They form very stout material about 10 inches in length and, like catgut, are absorbable in a wound. They are used for suturing large wounds in heavy muscle. Sterilisation is difficult but can be carried out as for catgut.

**Non-absorbable Ligatures.** The greatest use for this type of material is for suturing skin, but some surgeons prefer silk to catgut for internal operations although the silk will probably remain *in situ*. This preference is, in many cases, due to the fact that silk can be readily sterilised in the operating theatre.

Non-absorbable sutures should preferably have a smooth surface, be impermeable to water, resilient, and easy to remove after the healing of the wound. They are often coloured to contrast with the skin.

**Black horsehair** occurs in hanks, the threads being up to 28 inches in length. It is smooth and impermeable. It is occasionally used for small skin wounds, but is generally not very satisfactory as it is inclined to be brittle, particularly on the knots, whilst the gauge gradually decreases from the base to the tip. It may be sterilised by boiling or autoclaving.

**Silkworm gut**, so-called, has the same composition as ordinary silk, but a much wider gauge. Instead of being spun by the living silkworm it is extracted by the fingers from worms which have been killed. It is manufactured chiefly in Spain for this special purpose.

Silkworm gut occurs in hanks of 50 threads, the threads having an effective length of 10 to 14 inches. The gauges may be very fine, fine, medium, and stout, but being hand-prepared, the gauge may vary in the same thread. Silkworm gut is often supplied dyed in different colours, each colour representing a particular gauge, so that the surgeon can distinguish a mixture of threads of different gauges on the sterilising tray. Sterilisation may be carried out as for horsehair. It is employed as a substitute for catgut in deep-seated operations.

**Japanese synthetic gut** consists of silk thread specially surfaced and hardened by treatment with agar or some similar substance. It is a very stout material, very supple and smooth, and is supplied in a large variety of gauges. It occurs in lengths up to 40 yards. It may be sterilised as for horsehair and silkworm gut.

**Silk.** Ordinary silk thread slightly waxed is employed for long skin suturing, and very fine silk for suturing blood vessels, divided nerves and fascia. It is not advisable to use it where definite sepsis occurs, as it is liable to absorb contamination. It may be sterilised as for horsehair.

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## LINUM

(with PSYLLIUM, etc.)

*B.P., U.S.P. XI, P. Helv. V.*

The dried ripe seeds of *Linum usitatissimum* (Linaceæ). The seeds contain mucilage and about 30% of fixed oil. Preparations are administered for their demulcent action in the treatment of cough. The seeds, 1 or 2 teaspoonfuls in a tumbler of water, may be taken to increase the bulk of the intestinal contents in the treatment of constipation.

**Infusum Lini** (*B.P.C.*). *Syn.* LINSEED TEA.

*Dose.*—1 to 4 ounces (30 to 120 ml.). About 1 in 30.

**Linum Contusum** (B.P.). *Syn.* CRUSHED LINSEED, LINSEED MEAL. Coarsely powdered linseed, freshly prepared. Contains not less than 30% of oil.

**Mucilago Lini** (B.P.C.). 1 in 8.

**Oleum Lini** (B.P., U.S.P. XI, P. *Helv.* V, P. *Dan.*).

*Dose.*— $\frac{1}{2}$  to 1 ounce (15 to 30 ml.).

A yellowish-brown drying oil expressed from linseed. It thickens on exposure to air. Soluble 1 in 40 of dehydrated alcohol, slightly soluble in alcohol 90%; miscible with turpentine, ether, chloroform, carbon disulphide and light petroleum.

**Boiled linseed oil** is linseed oil heated with litharge, magnesium resinate or other "driers" causing the oil to dry more rapidly. It must not be used for linseed oil.

**Fœnum-græcum** (B.P.C., P. *Helv.* V) *Syn.* FŒNUGREEK. The seeds of *Trigonella Fœnum-græcum* (Leguminosæ), a herb largely grown in India and Egypt. The seeds contain a large proportion of mucilage and about 5% of oil, and are used chiefly in veterinary medicine. An Egyptian preparation, *Helba*, is made from fœnugreek—when soaked the seeds swell into a pasty condition and are used for fever, also for diabetes. Seeds which have been allowed to sprout for 3 or 4 days are sometimes preferred and are taken raw, together with un-sprouted seeds. A decoction of fœnugreek, an egg-cupful to a pint of water, boiled down to 5 oz., strained and taken cold on an empty stomach, has been used in diabetes.

**Ispaghula** (B.P.C.)

*Dose.*—45 to 150 grains. Pinkish-brown, boat-shaped seeds of *Plantago ovata* (Plantaginaceæ), containing mucilage and swelling in contact with moisture. Administered internally in intestinal atony, also in chronic diarrhœa, either dry, or as Decoctum Ispaghulæ (1½%) in doses of  $\frac{1}{2}$  to 2 ounces.

Has beneficial mechanical action in chronic dysenteries—R. N. Chopra, per *Med. Annu*, 1931, 159.

**Ispaghulæ Testa**, *syn.* ISPAGHULA HUSK, consists of the separated epidermis of the seeds. It is used in the same way as the whole seeds, but is more powerful in its action.

**Psyllium** (B.P.C.). *Syn. and Prop. Names.* FLEA SEED, ARCOLAX (Roberts, London), PSYLLA (Battle Creek Food Co., Michigan, Coates & Cooper, London).

The dried ripe seeds of *Plantago Psyllium* and of *P. arenaria* (Plantaginaceæ), from Southern Europe. Contain mucilage and are used in constipation, 1 to 4 teaspoonfuls or more being allowed to soak in half a cupful of water until a jelly is produced, the whole then being taken. The 1½% decoction is used in France as a demulcent drink.

**Coréine** (Daniel-Brunet, Boulogne-sur-Seine, Wilcox, Jozeau, London). Pure vegetable mucilage in flakes or granules. *Dose.*—2 teaspoonfuls thrice daily for constipation.

**I-so-gel** (Allen & Hanburys, London). The dried mucilage of certain tropical seeds in granular form. Aperient.

**Salep.** *Syn.* TUBERA SALEP (*P. Helv. V, P.G. VI, P. Ned. V, P. Belg. IV*). The dried tubers of *Orchis mascula* and other species of *Orchis* (Orchidaceæ). They are immersed in boiling water on collection and dried. They contain mucilage, and have nutritious and demulcent properties, allaying gastro-intestinal irritation. Mucilago Salep (*P.G. VI*) is 1% freshly made. Salep is much sold in the Indian bazaars as an article of diet.

**Angiolymphæ** (*Rous, Paris; C. Zimmermann, London*). Aqueous solution of glycosides of *Orchis maculata*, *Ixia rosea* and *Morea sinensis*. Administered by injection in the treatment of tuberculosis.

**Ulmus Fulva** (*B.P.C.*). *Syn.* SLIPPERY ELM. The dried inner bark of *U. fulva* (Ulmaceæ). It contains much mucilage and in powder is used as a demulcent. It should be free from starch. Ten grains shaken with an ounce of water should form a thick, jelly-like, fawn-coloured mass. Mixed with hot water, the powder is used as a poultice. Decoction.—1 in 8. *Dose.*—2 to 4 ounces. Glycogelatin pastilles are prepared containing 2 grains.

## LITHIUM

Li = 6.94.

Lithium salts have long had a reputation for assisting in the elimination of uric acid, but their effect is probably analogous to that of the corresponding potassium salts. They should be given freely diluted.

**Lithii Benzoas** (*B.P.C.*).  $C_6H_5COO Li = 128.0$ .

*Dose.*—5 to 15 grains (0.3 to 1 g.).

A light, white, crystalline powder or in scales. Antiseptic and diuretic.

*Soluble* about 1 in 3 of water, about 1 in 15 of alcohol 90%.

*Incompatible* with acids and sodium bicarbonate.

**Lithii Carbonas** (*B.P.C., P. Helv. V, P. Dan.*).  $Li_2CO_3 = 73.88$ .

*Dose.*—2 to 5 grains (0.12 to 0.3 g.) Tablets, 5 grains. A white amorphous or minutely crystalline powder.

*Soluble* 1 in 8 of water, 1 in 140 of boiling water, more soluble in water containing carbon dioxide; insoluble in alcohol. Diuretic, thought to increase the alkalinity of the blood.

**Lithii Chloridum** (*B.P.C.*).  $LiCl = 42.40$ .

*Dose.*—5 to 10 grains (0.3 to 0.6 g.).

White deliquescent crystals or crystalline powder, with salty taste.

*Soluble* 1 in  $1\frac{1}{2}$  of water, 1 in 30 of alcohol.

**Lithii Citras** (*B.P.C.*).  $C_2H_4OH(COOLi)_3, 4H_2O = 281.9$ .

*Dose.*—5 to 10 grains (0.3 to 0.6 g.). Tablets, 5 grains.

White crystalline powder. Diuretic.

*Soluble* 1 in 2 of water, insoluble in alcohol 90%.

**Lithii Citras Effervescens** (*B.P.C.*).

*Dose.*—1 to 2 drachms (4 to 8 g.). Contains 1 in 20.



**Lithii Gualacas.**

*Dose.*—5 grains (0·3 g.) in pill twice a day.

Prepared by digesting guaiacum resin in solution of lithium oxide, decanting the solution, evaporating, and scaling it. Contains lithium oxide 1, guaiacum resin 3. For gout and rheumatism.

**Lithii Hippuras.**  $C_6H_5 \cdot CO \cdot NH \cdot CH_2 \cdot COOLi, 2H_2O = 221 \cdot 0$ 

*Dose* —5 to 20 grains (0·3 to 1·2 g.)

In light, white, minute crystals, soluble 1 in 3 of water. Is a powerful solvent of calculi; useful in gout and rheumatism. Effervescent lithium hippurate contains 5 grains in 1 drachm.

**Lithii Sulphas.**  $Li_2SO_4, H_2O = 109 \cdot 9$ 

*Dose* —5 to 10 grains (0·3 to 0·6 g.)

White crystals soluble in water and alcohol

**Lithii Tartras Acidus.**

$CHOH \cdot COOLi \cdot CHOH \cdot COOH, 1\frac{1}{2}H_2O = 183 \cdot 0$

*Dose.*—5 to 20 grains (0·3 to 1·2 g.).

White crystalline powder, used in gouty cases with gum affections

**LOBELIA**

*B.P., P. Ital. V, P. Belg. IV, F E VIII, P Dan., P. Helv. V*

[P1] "*Alkaloids, the following; their salts, simple or complex — Lobelia, alkaloids of.*"

[81] "*Alkaloids, the following; their salts, simple or complex:— Lobelia, alkaloids of, except substances containing less than 0·5 per cent. of the alkaloids of lobelia.*"

[83] "*Alkaloids—Lobelia, alkaloids of—in preparations for the relief of asthma in the form of cigarettes, smoking mixtures or fumigants; substances containing less than 0·1 per cent of the alkaloids of lobelia.*"

[86] "*Alkaloids—Lobelia, alkaloids of—specify proportion as the proportion of any one alkaloid of lobelia that the preparation would be calculated to contain on the assumption that all the alkaloids of lobelia in the preparation were that alkaloid.*"

*Dose.*—1 to 3 grains (0·06 to 0·2 g.).

The dried aerial parts of *Lobelia inflata* (Campanulacæ) Has purgative and emetic properties in large doses, but its chief use is to relax spasm of the bronchi in asthma and bronchitis. It is contained in many anti-asthmatic powders (*vide Pulvis Lobeliæ Compositus*).

**Antidotes.** Treat as for poisoning by nicotine, *see* p. 650.

[P1] **Mistura Lobeliæ et Stramonii Composita** (*B.P.C.*).

*Dose.*— $\frac{1}{2}$  to 1 ounce (15 to 30 ml.).

Contains potassium iodide 5 gr., and ethereal tincture of lobelia 10 m., with ammonium carbonate and tincture of stramonium in chloroform water to 1 oz.

[P1] **Mist. Lobel. Co. (N I F).** Ethereal tincture of lobelia 10 m., potassium iodide 3 gr., mucilage of tragacanth 30 m., tincture of stramonium 20 m., water to  $\frac{1}{2}$  oz.

[P1] **Nebula Lobeliae Composita.** Tinctures of lobelia, belladonna and stramonium, of each 10 m., tincture of ipecacuanha 5 m., sodium nitrite 10 gr., glycerin and rose water to 1 oz.

**Pulvis Lobeliae Compositus (B.P.C.)** contains equal parts of lobelia, stramonium and tea impregnated with potassium nitrate and oil of anise.

**Pulvis Stramonii Compositus (B.P.C.)** contains stramonium 50%, with lobelia, anise and tea impregnated with potassium nitrate

The fumes of half a teaspoonful or more to be inhaled six or eight times a day. Himrod's and Potter's Asthma cures and proprietary asthma cigarettes resemble the above in composition (see Vol. II).

[P1] **Tinctura Lobeliae Ætherea (B.P.).**

*Dose* — 5 to 15 minims until nausea occurs.

1 in 5, prepared by percolation with spirit of ether.

[P1] **Tinctura Lobeliae Simplex (B.P.C.).** *Syn* TINCTURA LOBELIAE *Dose* — 10 to 30 minims (0.6 to 2 ml.).

1 in 8 in alcohol 60%. *I A.* agreed 10% w/w in alcohol 70%.

[P1 81] **Lobeline.**  $C_{22}H_{27}O_2N = 337.2$ .

A crystalline alkaloid obtained from lobelia. A powerful respiratory stimulant, but should be used cautiously in patients with enfeebled myocardium. Probably more effective combined with a cardiac stimulant. Is usually used as the hydrochloride. For pharmacology see F R Curtis and S. Wright, *Lancet*, 11/1926, 1255.

[P1 81] **Lobelinum Hydrochloricum (P.G. VI, P Belg. IV, P. Helv. V)**  $C_{22}H_{27}O_2N.HCl = 373.7$ .

*Max dose* —  $\frac{1}{2}$  grain (0.02 g.): *per diem* 1  $\frac{1}{2}$  grains (0.1 g.). *P. Helv. V* has  $\frac{1}{8}$  and  $\frac{1}{4}$  grain respectively.

Intravenously  $\frac{1}{8}$  grain (10 mg.) in 1% solution

A white crystalline powder, soluble 1 in 50 of water, 1 in 10 of alcohol; easily soluble in chloroform. *Solutions must not be heated.*

**Used** as respiratory stimulant in emergencies, also in coal gas poisoning and in acute morphine poisoning

[P1] **Lobelin Ingelheim (Boehringer, Hamburg, Zimmermann, London).** Solution of lobeline hydrochloride in 1 ml ampoules containing  $\frac{1}{10}$  grain (0.01 g.) or  $\frac{1}{20}$  grain (0.003 g.). *Dose.*—Subcutaneously for adults and for older children,  $\frac{1}{10}$  grain, for new-born infants,  $\frac{1}{20}$  grain intramuscularly. The effect sets in after  $\frac{1}{2}$  to 1 minute, but is of short duration. Injections may be repeated every 2 to 4 hours. In particularly urgent cases  $\frac{1}{20}$  gr. may be given by slow intravenous injection, and is effective in 3 to 6 seconds.

**MAGNESIUM**

Mg = 24.32.

**Magnesium Carbonas Levis** (*B.P.*, *P. Helv. V*, *P. Dan.*).*Dose*.—10 to 60 grains (0.6 to 4 g.).

Prepared by boiling together dilute solutions of magnesium sulphate and sodium carbonate. The composition corresponds approximately to  $3\text{MgCO}_3, \text{Mg}(\text{OH})_2, 3\text{H}_2\text{O}$ .

**Magnesium Carbonas Ponderosus** (*B.P.*).*Dose*.—10 to 60 grains (0.6 to 4 g.).

Prepared by mixing boiling concentrated solutions of magnesium sulphate and sodium carbonate, evaporating to dryness and washing out the sulphate. The composition corresponds approximately to  $3\text{MgCO}_3, \text{Mg}(\text{OH})_2, 4\text{H}_2\text{O}$ .

**Magnesium Carbonas** (*U.S.P. XI*).*Average dose*.—As antacid 10 grains, as laxative 2 drachms.

Described as a bulky white powder or as light white friable masses. Contains the equivalent of about 40% of MgO.

**Sippy's Powder.***Dose*.— $\frac{1}{2}$  to 2 drachms (2 to 8 g.) in water.

No. 1—Magnesium carbonate and sodium bicarbonate equal parts.

No. 2—Calcium carbonate and sodium bicarbonate equal parts.

Sippy's method of treating gastric ulcer was by checking acidity of the gastric juice to prevent further corrosive action. Cf. Maclean's Powder, p. 284.

**Liquor Magnesium Bicarbonatis** (*B.P.*). *Syn.* FLUID MAGNESIA. *Dose*.—1 to 2 ounces (30 to 60 ml.).

A colourless liquid saturated with carbon dioxide and containing not less than 2.5% *w/v* of  $\text{Mg}(\text{HCO}_3)_2$ , equivalent to about  $7\frac{1}{2}$  grains of magnesium carbonate in 1 oz.

It can be made in a Sparklet syphon as follows:—Add a boiling solution of magnesium sulphate 40 g. in water 200 ml. to a cold solution of sodium carbonate 50 g. in water 200 ml.; boil until carbon dioxide is removed, collect the precipitate on a calico strainer, wash until free from sulphate, suspend in 400 ml. of water and transfer to a "C" size Sparklet syphon. Discharge a bulb of gas into the liquid, shake and allow to stand for 6 hours. Discharge a second bulb, shake and allow to stand for 18 hours.—G. R. Gibbon, *Pharm. J.*, 11/1934, 403.

**Liquor Magnesium Citratis** (*B.P.C.*). LIMONADE PURGATIVE AU CITRATE DE MAGNÉSIE (*Fr. Cx.*).

*Dose*.— $3\frac{1}{2}$  to 10 ounces (100 to 500 ml.), or more.

A solution containing magnesium citrate, saturated with carbon dioxide and flavoured with lemon.

**Liquor Magnesium Citratis** (*U.S.P. XI*). *Average dose*.—7 ounces (200 ml.).

Prepared by dissolving magnesium carbonate in a hot solution of citric acid, adding syrup and heating to boiling point, adding oil of lemon mixed with talc and filtering while hot into a strong bottle; after diluting to the required volume and cooling, potassium or sodium bicarbonate is added, the bottle securely stoppered, and kept on its side in a cool place, preferably in a refrigerator.

[P1] **Mistura Magnesii et Belladonnæ (C.X.H.).** *Syn.* MISTURA GASTRICA.

Light magnesium carbonate 10 gr., bismuth carbonate 10 gr., tincture of belladonna 7½ m., sodium citrate 15 gr., peppermint water to 1 oz. For hyperacidity and peptic ulcer. To be taken 3 or 4 times a day, the last dose being increased to 1½ or 2 oz.

**Magnesii Hydroxidum (B.P.C.).**  $\text{Mg}(\text{OH})_2 = 58.3$ .

*Syn.* MAGNÉSIE HYDRATÉE (*Fr. Cx.*).

*Dose.*—10 to 60 grains (0.6 to 4 g.), or more. Usually administered as *Mistura Magnesii Hydroxidi* (*vide infra*).

Prepared by decomposition of magnesium sulphate 24½ with sodium hydroxide 8 in solution, the precipitate being washed free from sulphate and dried at a low heat

According to the *Fr. Cx.*, calcined magnesia is boiled with 20 to 30 times its weight of distilled water 20 minutes. Dry as much as possible by collecting on calico and finally at 50° until it no longer loses weight. Thus prepared, magnesium hydroxide contains 31% of water.

It dissolves more freely in dilute acids than calcined magnesia and is preferred to the carbonates as an antacid since no carbon dioxide is liberated. It is a recognised antidote in arsenical poisoning.

[P2] **Lotio Magnesii Hydroxidi et Phenolis (St. Mark's H.).**

Phenol 15 gr., zinc oxide 30 gr., calamine 15 gr., glycerin 30 m., rose water 60 m., mixture of magnesium hydroxide to 1 oz

**Mistura Magnesii Hydroxidi (B P).** *Syn.* CREAM OF MAGNESIA, CREMOR MAGNESIÆ.

*Dose.*—1 to 4 drachms (4 to 16 ml.). Four drachms contains the equivalent of about 12½ gr of magnesium oxide.

An aqueous suspension of hydrated magnesium oxide containing the equivalent of about 8.25% of  $\text{Mg}(\text{OH})_2$ . Antacid without evolving carbon dioxide.

*Uses.* In indigestion, dyspepsia, acidity, rheumatism, and as an alkaline mouth-wash. A useful antidote in case of poisoning by mineral acids.

**Magma Magnesiae (U.S.P. XI)** Contains 7 to 8.5% of  $\text{Mg}(\text{OH})_2$ . No method of preparation is given, and the solution may contain 0.1% of citric acid to minimise its action on glass, and 0.05% of volatile oil for flavouring purposes.

**Pulvis Magnesii Hydroxidi cum Carbone.**

*Dose.*—1 to 2 drachms in a little water after meals.

Magnesium hydroxide 1, charcoal 2.

Is suggested in dyspepsia. The magnesium hydroxide is antacid and the charcoal has the property of gas absorption.

A little cinnamon powder (1 in 8) is occasionally added.

**Alkagen Tablets (Allen & Hanburys, London).** Contain magnesium hydroxide 4 gr. and peppermint oil 1 m. *Dose.*—1 to 3 with water. For acidity, flatulence, etc. Lozenges, and granules containing 75% of glucose are also available

[P1] **Sedogastrine (Bengué, London).** Magnesium hydroxide, calcium carbonate, sodium and calcium phosphates, and conium, in granules and tablets for hyperacidity, dyspepsia, etc

**Magnesii Lactas.**  $(\text{C}_2\text{H}_5\text{OH COO})_2\text{Mg} \cdot 3\text{H}_2\text{O} = 256.4$ .

*Dose.*—15 to 60 grains (1 to 4 g.). White crystalline powder. Soluble 1 in 30 of water; insoluble in alcohol 90%.

A mild laxative. Useful in some cases as a hæmostatic where calcium salts do not seem to act. A dose of 30 grains usually reduces time of coagulation of the blood 30%, e.g., from 2 to 1½ minutes. The salt can be made extemporaneously by the dispenser, if prescribed in a mixture, from magnesia 1, with lactic

acid about 5. The large dose of the bulky powder, if ordered in that form, is inconvenient to take.

**Magnesi Oxidum Leve** (B.P.), *syn.* MAGNESIA LEVIS, MAGNESII OXIDUM (U.S.P. XI), and **Magnesi Oxidum Ponderosum** (B.P.), *syn.* MAGNESIA PONDEROSA.  $\text{MgO} = 40 \cdot 32$ .

*Doses.*—As for the carbonates U.S.P. XI has average dose as antacid 4 grains, as laxative 45 grains.

These are prepared from the respective carbonates by exposure to a dull red heat. Antacid, antilithic, diuretic, laxative.

Magnesia should never be prescribed as compressed tablets since these do not dissolve and may form the nucleus of calculi —Per *Pharm. J.*, i/1925, 470.

**Magnesi Phosphas** (B.P.C.). *Syn.* TRIBASIC MAGNESIUM PHOSPHATE. *Dose.*— $\frac{1}{4}$  to 1 drachm (1 to 4 g.)

A white, slightly gritty powder consisting of a hydrated tribasic phosphate containing about 30% of combined water. Products containing more water are liable to become fungoid.

*Used* as an antacid. Does not produce systemic alkalinisation. Has laxative action.

**Magnesi Sulphas** (B.P., U.S.P. XI).  $\text{MgSO}_4 \cdot 7\text{H}_2\text{O} = 246 \cdot 5$ . *Syn.* EPSOM SALTS, SEL ANGLAIS (P. Belg. IV), SEL D'ANGLETERRE, SEL DE SEDLITZ (Fr. Cx, P. Helv. V, P. Dan.).

*Dose.*— $\frac{1}{4}$  to 4 drachms (2 to 16 g.).

Death following ingestion of 57 g. Care should be exercised as toxicity may result without death—idiosyncrasy may exist and the average dose may be toxic. If toxicity does occur use calcium salts subcutaneously or intravenously —H. S. Thatcher, *J. Amer. med. Ass.*, ii/1928, 1185.

In colourless crystals with a saline bitter taste.

*Soluble* 10 in 13 of water—measuring 18.5 (B.P. gives 1 in  $1\frac{1}{2}$ )

*Incompatible* with Soda Tartarata, alkali carbonates and bicarbonates unless in dilute solution. With potassium or ammonium bromide concentrated solutions give a precipitate of the double sulphate.

#### **Pharmacology.**

This salt *per os* does not act by attracting fluid into the intestine, since the watery stool following ingestion contains none of the salt. This is passed in the solid stool on the following day. It is suggested that its purgative action depends upon a duodeno-colic reflex analogous to the similar but less painful reflex produced by food.—*Med. Pr.*, 1926, July 14.

*Intravenously* in large doses it is toxic and may produce death. The dose should not exceed 0.1 g. per kilo weight and should not be given in a concentration exceeding 10%.—H. J. Stander, *J. Amer. med. Ass.*, i/1929, 636.

*Uses.* Largely employed as an efficient evacuant. Externally, it is used in baths for rheumatic affections and the saturated solution has been applied for its anæsthetic effect in arthritis, orchitis and other inflammatory conditions. Intraspinal injections of 2.5 to 6 ml. of a 25% solution have been used successfully in the treatment of tetanus and the 10% solution has been given intravenously in doses of 10 to 25 ml. in eclampsia.

**ANGIOSPASM.** A spastic condition of the arterial wall which may affect any part of the arterial tree right down to the capillaries. Cases of intermittent claudication, endarteritis obliterans, Buerger's disease, migraine, spasm of the brachial artery, acute pulmonary oedema, angina pectoris, coronary thrombosis

and cerebral angiospasm have all been treated with varying success by magnesium sulphate intravenously. The patient lies on a couch with head and shoulders slightly raised and a solution of magnesium sulphate and glucose is slowly injected. The dose is 5 to 10 ml. of a 20% solution and an equal volume of 10% to 40% glucose. About half a minute after commencement of injection the patient feels intense heat all over the body. Treatment usually given twice weekly. Magnesium sulphate probably relaxes vascular spasm by direct action on the vasomotor centre of the brain—N Pines, *Lancet*, 1/1933, 577.

**DEAFNESS** Hot baths containing 1 lb. of magnesium sulphate are sometimes effective in a minority of chronic cases. To be used with caution in elderly people. 10 minutes' immersion enough. Exhausting—J. Adam, *Brit. med. J.*, 1/1931, 621.

**ECLAMPSIA** Intravenously, 10 to 25 ml. of a 10% solution, gave good results. Convulsions controlled, oedema reduced and diuresis promoted—*Amer. J. Obstet. Gynec.*, Feb., 1925. See also H. Pritchard, *Brit. med. J.*, 1/1928, 794.

The preceding intravenous dose, or 15 ml. of 25% intramuscularly, repeated at intervals of 2 hours—*Brit. med. J. Epist.*, 1/1930, 63.

5 to 10 ml. of 25% solution intramuscularly after each convulsion, until controlled. It is not used in coma. Give colonic irrigation, wash out stomach, and leave 60 ml. of saturated magnesium sulphate in it. Then inject 1000 ml. of 20% dextrose solution during 30 to 50 minutes 2, 3, or 4 times daily. When stomach has emptied itself, inject 5% syrup water, beginning with 50 ml. and increasing hourly up to patient's tolerance, possibly up to 300 ml. an hour, until patient is conscious—O. H. Schwarz, *J. Amer. med. Ass.*, 11/1929, 1679.

**EPIDEMIC ENCEPHALITIS** greatly benefited by magnesium sulphate, 4 ml. of a 25% solution, intramuscularly—E. Matthew, *Lancet*, 1/1924, 1156.

**ERYSIPELAS.** A cold saturated aqueous solution of magnesium sulphate, containing 10 to 20% of glycerin, favoured.—W. T. Benson, *Lancet*, 11/1930, 1286.

**HEADACHE**, e.g., post-concussional, 4 to 8 oz. of 50% magnesium sulphate solution per rectum.—A. Feiling, *Brit. med. J.*, 11/1930, 907.

**HYPOPYON ULCERS** treated with magnesium sulphate lotion—up to saturated solution. Encouraging—D. Matheson Mackay, *Brit. med. J.*, 11/1921, 738.

**MENTAL CASES.** 2 ml. of 50% solution injected as sedative. In 82.7% of cases the action was prompt, the patient becoming quiet in 13 to 30 minutes and then sleeping from 5 to 7 hours—*Med. Pr.*, 1/1923, 291.

**OTORRHOEA.** Cleanse the meatus. Half fill the meatus with powdered magnesium sulphate (cryst.) and cover with a large piece of wool. Where discharge is free, four-hourly treatment is needed, otherwise once or twice a day suffices. As a rule the ear is dry in three weeks or less and hearing is greatly improved—E. Watson-Williams, *Brit. med. J.*, 11/1933, 49.

**RODENT ULCER** of the face healed after 5 injections of magnesium sulphate.—R. W. Moir, per *Prescriber*, 1923, 237.

**SYDENHAM'S CHOREA.** Intramuscular injections of a 25% aqueous solution most effective. In children of 1 to 5 an injection of 5 ml. is given deeply into the gluteal muscles every 2 days, and in older children 10 ml. In most cases improvement occurs after the second to the fifth injection, with cure after the tenth. Severe cases were often cured more rapidly than milder ones. No secondary effects and no renal or cardiac complications—M. R. Couterras, *Pr. méd.*, 1/1936, 228.

**TROPICAL ULCER** treated with wet dressings of magnesium sulphate 25% solution—J. F. James, *Indian med. Gaz.*, June, 1925, 274.

**ULCERS** of the leg treated by soaks of 5 to 10% magnesium sulphate solution—J. H. Young, *Lancet*, 1/1929, 976.

**URÆMIA** successfully treated by slow intravenous infusion of a 1% solution (2 g.  $MgSO_4 \cdot 7H_2O$  in 100 ml. of distilled water). Indicated when blood pressure rises above 130 mm.—C. B. Watson, *Brit. med. J.*, 11/1931, 1086.

**Balneum Magnesii Sulphatis (B.P.C.)** Contains 1 lb. of magnesium sulphate per 30 gallons.

**Enema Magnesii Sulphatis (B.P.C.).** Dose.—20 ounces (600 ml.). 5% w/v in mucilage of starch with olive oil 10% v/v.

**Liquor Magnesii Sulphatis** (*R.I. Edin.*). *Syn.* HENRY'S SOLUTION.

*Dose.*— $\frac{1}{2}$  to 1 ounce (15 to 30 ml.).

Magnesium sulphate  $\frac{1}{2}$  oz., dilute sulphuric acid 20 m., water to 1 oz. An occasional purge.

**Magnesii Sulphas Effervescens** (*B.P.C.*). *Dose.*— $\frac{1}{2}$  to 1 ounce (15 to 30 g.), or 1 to 3 drachms (4 to 12 g.) repeated.

Contains about 50% of magnesium sulphate which, in this form, is frequently more effective, and more palatable.

**Mistura Alba** (*B.P.C.*). *Dose* — $\frac{1}{2}$  to 1 ounce (15 to 30 ml.).

Magnesium sulphate 120 gr. and light magnesium carbonate 20 gr. in peppermint water to 1 ounce. A mild aperient

BLOOD PRESSURE, TO REDUCE. In uncomplicated hypertony give *Mistura Alba* as routine treatment. Drinking large quantities of water often beneficial.—I. Harris, *Lancet*, ii/1931, 1045.

[P1] **Mistura Salina Laxans** (*St. T. H.*). Magnesium sulphate 30 gr., potassium citrate 20 gr., tincture of hyoscyamus 15 m., chloroform water to 1 oz

**Magnesii Sulphas Exsiccatus** (*B.P.C.*, *P. Helv. V*, *P. Dan.*).

*Dose.*— $\frac{1}{2}$  to 3 drachms (2 to 12 g.).

Prepared by heating magnesium sulphate at 100° until it has lost 25% of its weight. A white powder soluble 1 in 2 of water. Contains 62 to 70% of  $MgSO_4$ .

**Pasta Magnesii Sulphatis** (*B.P.C.*). *Syn.* MORISON'S PASTE

Prepared with magnesium sulphate dried to constant weight at 100°, when the loss in weight is about 37%, by mixing  $4\frac{1}{2}$  parts with  $5\frac{1}{2}$  parts, by weight, of glycerin and incorporating 0.5% of phenol.

Morison's original formula was prepared by mixing  $1\frac{1}{2}$  lb. of exsiccated magnesium sulphate with 11 ounces of glycerin of phenol (the phenol may be omitted). The exsiccated magnesium sulphate used was "in the form of a fine white powder containing 12% less water than the ordinary."—(See A. E. Morison, *Brit. med. J.*, i/1924, 703; also *ibid.*, i/1918, 342)

Was originally advocated for the treatment of wounds, later for boils and carbuncles. For wounds the dressing of gauze and wool is left unchanged for 6 to 8 days unless more wool is required, and after a few such dressings a magnesium sulphate solution is applied. The paste is applied to boils, carbuncles, etc., until a slough has separated.

**Pasta Mag. Sulph.** (*N.I.F.*). Exsiccated magnesium sulphate 2 oz., glycerin 1 oz. (by weight).

**Sterules Magnesium Sulphate** (*Martindale, London*) contain 1 ml. of 50% magnesium sulphate solution for use in conjunction with rectal ether anaesthesia in obstetrics.

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## MALTUM

*Syn.* CEBADA GERMINADA (*F.E. VIII*)

Grain of barley partially germinated artificially and then dried. Yields 70% extract.

**Malti Pulvis.** *Dose.*—1 to 2 drachms (4 to 8 g.).

Malt flour or entire malt powdered, is added to baked wheaten flour in various proportions to form the popular infants' foods, and is given to assist digestion. When these are mixed with hot water or a mixture of hot milk and water, the starch contained in the wheaten flour becomes soluble and digested into dextrin and malt sugar. The diastasic property of malt is most active in aqueous solution at 104°F.,—a boiling heat destroys it. A small teaspoonful of malt flour may be sprinkled over or mixed with cooked farinaceous foods, coffee, beer, etc.

**Extractum Malti (B.P.).** *Syn.* EXTRACTUM BYNES, EXTRAIT D'ORGES. DIAMALT (*British Diamalt Co., Sawbridgeworth*), KEPLER (*Burroughs Wellcome, London*), and MALTINE (*Glaxo Laboratories, London*) are proprietary brands of extract of malt. (*Note.*—Maltine in France is a synonym for diastase.)

*Dose.*—1 to 4 drachms (4 to 16 ml.).

A brownish, semi-liquid substance, sp. gr. 1.40 to 1.42, with pleasant sweet taste, consisting principally of maltose (about 50%), with dextrin, dextrose, diastase, protein, phosphates and aromatic principles. The B.P. requires a nitrogen content equivalent to 4.5% w/w of protein. It is made by mixing malt with tepid water (55°), pressing, filtering, and evaporating *in vacuo* at below 55°. Extract of malt and its preparations are prescribed in cases of debility of all kinds, as a restorative, but particularly where digestion is weak. Commercially, malt extracts are assayed for their diastasic power (Lintner value) but since diastase is inactive *per os* no such assay is required by the B.P.

#### **National Mark (Pharmaceutical) Malt Extract.**

Under the Agricultural Produce (Grading and Marking) Act, 1928, and the Malt and Flour and Malt Extract Regulations, 1929, All-English Pharmaceutical Malt Extract is prescribed made from home-grown barley (For details, see Vol. II.)

**Extractum Malti (U.S.P. XI).** *Average dose*— $\frac{1}{2}$  oz. (15 g.).

It can convert not less than five times its weight of starch into water-soluble sugars, and unlike the product of the British Pharmacopœia its diastasic activity is regarded as the factor of primary importance.

F.E. VIII incorporates 10% of glycerin and the finished product must digest five times its weight of potato starch at 40°.

#### **Extractum Malti cum Oleo Morrhue (B.P.).**

*Dose.*—1 to 4 drachms (4 to 16 ml.).

Contains 10% w/w of cod-liver oil, equivalent to approximately 15% v/v.

#### **National Mark All-English (Pharmaceutical) Malt Extract with Cod-liver Oil.**

Under the Agricultural Produce (Grading and Marketing) Act, 1928, and the Malt and Flour and Malt Extract Regulations, 1929, All-English Malt Extract may be mixed with not less than 15% by volume of cod-liver oil of B.P. quality with permissible variation of 1%.



**Extractum Malti cum Oleo Olivæ (B.P.C.)**

*Dose.*—1 to 2 drachms (4 to 8 ml.).

Olive oil 15% *v/v* in extract of malt.

**Extractum Malti Ferratum (B.P.C.).**

Soluble iron pyrophosphate  $1\frac{1}{2}$  dissolved in water and mixed with extract of malt.

*Dose.*—1 to 4 drachms (4 to 16 ml.).

**Extractum Malti Liquidum (B.P.C.).**

*Dose.*—1 to 4 drachms (4 to 16 ml.)

In place of evaporating malt infusion to the viscosity of the soft extract, it is concentrated *in vacuo* until it has sp gr 1.375, and about 10% of alcohol added, making the finished product of sp. gr. about 1.23. It may also be prepared by diluting the soft extract ( $67\frac{1}{2}\%$  *v/v*) with alcohol and water.

**Extractum Malti Liquidum cum Cascara.**

*Dose.*—1 to 4 drachms (4 to 16 ml.) Liquid extract of cascara 1, liquid extract of malt 7. This is palatable. Mix and mark "Shake"

**Extractum Malti Liquidum cum Glycerophosphatibus (B.P.C.).** *Dose.*—1 to 4 drachms (4 to 16 ml.)

Contains 2 gr. each of sodium and potassium glycerophosphates in 4 dr.

**Extractum Malti Liquidum cum Hæmoglobino (B.P.C.).**

*Dose.*—1 to 4 drachms (4 to 16 ml.). Contains 30 gr. of hæmoglobin in 4 dr.

**Extractum Malti Liquidum cum Hypophosphitibus (B.P.C.).** *Dose.*—1 to 4 drachms (4 to 16 ml.)

Contains 1 gr. each of calcium and sodium hypophosphites in 4 dr.

**Extractum Malti Liquidum cum Pancreatina.** *Dose.*—1 to 4 drachms (4 to 16 ml.)

Liquid extract of malt 2, solution of pancreatin 1

**[P1] Extractum Malti Liquidum cum Quinina et Strychnina (B.P.C.).** *Dose.*—1 to 4 drachms (4 to 16 ml.).

Contains quinine hydrochloride  $\frac{1}{2}$  gr and strychnine hydrochloride  $\frac{1}{4}$  gr. in 4 dr.

**Extractum Malti cum Vitaminis (B.P.C.)**

*Dose.*— $\frac{1}{2}$  to 1 ounce (8 to 30 ml.)

Contains solution of vitamin A and solution of irradiated ergosterol and is about three times as potent as extract of malt and cod-liver oil. 1 dr. contains about 3000 units of vitamin A and 225 units of vitamin D.

**Extractum Malti Liquidum et Medullæ Rubræ (B.P.C.)**

*Dose.*—1 to 4 drachms (4 to 16 ml.).

Equal parts of liquid extract of malt and extract of red bone marrow.

**Extractum Malti Siccum.**

Contains about 75% maltose, 1.5% phosphates, 5% albuminoids. *Dose*.—1 to 2 drachms.

A somewhat hygroscopic yellowish coarse powder, easily soluble in water. Is desiccated *in vacuo* and keeps well

**Dry Malt Extract with 50% Paraffin.**

*Dose*.—Infants, one teaspoonful dissolved in slightly warmed milk feed three times a day. Children, two teaspoonfuls two or three times a day. Adults, one tablespoonful three or four times daily. Best taken just before or after meals.

**Mistura Ferri cum Malto (B.P.C.).**

*Dose*.—1 to 2 dr. (4 to 8 ml.).

Contains 3 gr of soluble iron pyrophosphate per dr

**Bronamalt** (*Fletcher, Fletcher & Co, London*) A combination of a hydrobromic extract of cinchona with a liquid malt *Dose*—1 to 2 drachms with or immediately after meals In cases of impaired nutrition and loss of appetite, especially in children.

**Bynin** (*Allen & Hanburys, London*) A brand of liquid extract of malt. Also available in numerous combinations including liquid paraffin, glycerophosphates, hæmoglobin, liver extract, stomach extract, hypophosphites, lecithin, pancreatin and phosphates [P1] **Bynin Amara** contains in 1 oz quinine phosphate 1½ gr, iron phosphate 2 gr, strychnine phosphate ⅛ gr, in liquid extract of malt.

**Jecomalt** (*Wander, London*). A dry extract of malt with cod-liver oil, in yellow granular powder

**Ostomalt** (*Glaxo Laboratories, London*) Standardised concentrated malt preparation of vitamins A, B complex, C and D, with calcium glycerophosphate

**Radio-Malt** (*British Drug Houses, London*) A malt extract preparation containing vitamins A, B<sub>1</sub>, B<sub>2</sub> and D

**Diastasum (B.P.C.) Syn AMYLASE.**

*Dose*.—1 to 5 grains (0.06 to 0.3 g.)

An enzyme obtained from an infusion of malt, prepared at below 60°, by precipitation with alcohol. Occurs as a yellowish or whitish amorphous powder, almost entirely soluble in water. Converts starch into sugars and dextrin, and is used in amylaceous dyspepsia in conjunction with pepsin

**Luizym** (*Luitpold-Werk, Munich; Medical Laboratories, London*) A digestive enzyme preparation containing cellulase, hemicellulase, amylases, proteases and esterases in tablets For digestive disturbances

**Taka-Diastase** (*Parke, Davis, London*). Amylolytic enzyme derived from species of *Eurotium oryzae* cultivated on wheat bran *Dose*—5 grains For the treatment of amylaceous dyspepsia

**Takazyma** (*Parke, Davis, London*) Powder containing magnesium carbonate, bismuth carbonate, Taka-Diastase, calcium carbonate and aromatics. *Dose*.—1 to 2 teaspoonfuls in water. For hyperchlorhydria.

**Maltosum (B.P.C.).**  $C_{12}H_{22}O_{11}, H_2O = 360.2$ 

Consists of  $\beta$ -maltose obtained from starch by hydrolysis with diastase. Crystallises from water as the monohydrate, from alcohol as the anhydrous substance. Used in bacteriological culture media.

**Dextri-Maltose.** (*Mead, Johnson & Co, Evansville; Brooks & Warburton, London*). A powder containing 51% of maltose, 42% of dextrin and 5% of water and, at choice, salt free, or containing sodium chloride 2% or potassium bicarbonate 3%. No. 1 (with salt) is for infant feeding, No. 3 (with potassium bicarbonate) for infants who suffer from constipation. No. 2 (salt free) for use by practitioners who prefer to make their own salt additions.

**Malto-Dextrin** (*Glaxo Laboratories, London*). A mixture of dextrans, malto-dextrans and maltose for modifying milk mixtures; it contains no unaltered starch. Composition approx. 50% of maltose and 50% of dextrin and malto-dextrin.

## MANGANUM

Mn = 54.93.

**MANGANESE POISONING**—cases described—*Per Clin. J.*, May, 1923, 233.

Poisoning due to inhalation of dust while grinding the ore.—R. F. Gayle, *J. Amer. med. Ass.*, ii/1925, 2008.

A report of 4 cases of chronic manganese poisoning in men working in the same manganese works, the symptoms appearing in one case after only 8 months' work and in the other three after 2½, 6½, and 8 years respectively. Clinical picture indistinguishable from chronic post-encephalitic parkinsonism; signs and symptoms of hepatic cirrhosis not found.—D. Owen, *Brit. med. J.*, ii/1934, 833.

**Mangani Butyras.**  $(C_3H_7\cdot COO)_2Mn = 229.0$ .

**Dose.**—1 to 1.5 ml. of 1% solution intramuscularly—not more than 3 injections should be given with 3 or 4 days' clear interval between them.

A pale pink powder having only a slight odour of butyric acid. Is precipitated as a heavy oily liquid by interaction of solutions of sodium butyrate and manganese chloride. This oil is washed with water, dried over sulphuric acid, and then washed with ether to remove free butyric acid. The product is again dried over sulphuric acid for some days, and powdered.

**Soluble** 1 in about 6 of water. The substance is hydrolysed by boiling water with deposition of manganese hydroxide.

**Uses.** Boils, carbuncles, erysipelas, whitlows, lymphangitis, lymphadenitis, gonococcal urethritis and abscess formation have been treated by manganese butyrate solution (1%). The addition of sodium thiosulphate ½ gr. to the solution has been stated to reduce the pain of the injection.

In gonorrhœa, the drug "par excellence." Intramuscularly into the buttocks on the first and fifth day of the discharge, in doses of 1 ml and 1.5 ml of 1% solution. Results extremely gratifying, the acute stage of the disease being materially lessened. Only two injections should be given.—J. J. Abraham, *Lancet*, i/1924, 1224.

Staphylococcal and streptococcal infections better treated than gonorrhœal. It will ward off an attack of rhinitis, influenza, and other infections, providing it is used early. Also used in dermatitis, asthma, and urticaria.—*See also* J. E. R. McDonagh, *Brit. med. J.*, i/1925, 655.

**BOILS.** The most satisfactory treatment for boils, recurring or non-recurring, is intramuscular injections of manganese butyrate. Moist dressings are unnecessary.—H. L. McCormick, *Brit. med. J.*, ii/1932, 780. Value confirmed—A. P. Bertwistle, *ibid.*, 904.

**MINERS' BOILS AND CARBUNCLES** Manganese injections recommended—S. W. Fisher, *Lancet*, i/1931, 750.

**VASCULAR HYPERTENSION AND HYPOTENSION.**—Hypertension and hypotension are stated to be caused by changes in the nature of the protein particles of the plasma.

Hypertension is a result of the protein particles leaving the colloidal state and forming true solutions, and is found in cases of chemical intoxication, in some cases of syphilis and diabetes, in pregnancy and at the menopause, and is the natural sequence of old age. The best remedy for acute cases is the injection of 1% manganese butyrate solution in doses of 1, 0.5, 2.0 ml. at five-day intervals. In chronic cases, insulin 20 units is a suitable drug. With all these methods the course may have to be repeated.—J. E. R. McDonagh, *Med. Pr.*, Jan. 23 and 30, 1924.

**Mangani Chloridum.**  $\text{MnCl}_2, 4\text{H}_2\text{O} = 197.9$ .

*Dose.*—5 grains (0.3 g.);  $\frac{1}{4}$  to  $\frac{1}{2}$  grain by injection (0.016 to 0.03 g.).

Rose coloured deliquescent crystals, soluble about 1 in 1 of water, and in alcohol 90%.

**DEMENTIA PRÆCOX** (but not cases with active organic disease) treated by 30 half-weekly injections intravenously of from 2 to 8 ml. of a 0.02% solution, then 0.3 g. manganese chloride *per os* twice daily for a month. Improves physical condition, but optimum intravenous dose should not be exceeded.—G. E. Reed, *per Med Annu*, 1931, 316

**Mangani Citras**, "Soluble."

*Dose.*—3 to 5 grains (0.2 to 0.3 g.).

This, a double salt with sodium citrate, and Ferro-Mangani Phosphas.—*Dose.*—3 to 10 grains (0.2 to 0.6 g.)—are scale preparations.

**Mangani Hypophosphis.**  $\text{Mn}(\text{H}_2\text{PO}_2)_2, \text{H}_2\text{O} = 203.0$ .

*Dose.*—1 to 5 grains (0.06 to 0.3 g.).

A white or slightly rose-tinted powder, soluble 1 in 7 of water.

A nerve stimulant.

**Mangani Dioxidum Præcipitatum** (*B P C*)  $\text{MnO}_2 = 86.93$  *Syn.* MANGANI PEROXIDUM PRÆCIPITATUM.

*Dose.*—2 to 8 grains (0.12 to 0.5 g.) or more, in pills with syrup. Tablets, 2 grains (0.12 g.)

A bulky blackish brown powder, free from grittiness and entirely soluble in cold hydrochloric acid

Contains not less than 80% of  $\text{MnO}_2$ .

*Uses.* In gastrodynia, pyrosis, and in amenorrhœa taken 3 or 4 times a day before expected period. In chlorosis it assists the action of iron salts, and is less irritant than the permanganates

**Mangani Phosphas.**  $\text{Mn}_3\text{P}_2\text{O}_8, 7\text{H}_2\text{O} = 480.9$

*Dose.*—1 to 5 grains (0.06 to 0.3 g.)

A white powder, generally with a pinkish tint, insoluble in water

**Mangani Sulphas.**  $\text{MnSO}_4, 4\text{H}_2\text{O} = 223.1$  *Syn.* SULFATO DE MANGANESO (*F.E. VIII*). *Dose.*—2 to 10 grains (0.12 to 0.6 g.)

A white powder with a faint pink tint, due to a little manganic sulphate, or in pink crystals. Soluble about 1 in  $1\frac{1}{4}$  of water.

Given in conjunction with iron in anæmia.

**Potassii Permanganas** (*B P.*, *U.S.P. XI*, *P. Helv. V*, *P. Dan.*)  $\text{KMnO}_4 = 158.0$ .

*Dose.*—1 to 3 grains (0.06 to 0.2 g.) in well-diluted solution, or in pill. *U.S.P. XI* average dose 1 grain.

In purple crystals with astringent taste, soluble about 1 in 20 of water.

**Incompatible** with all vegetable oxidisable matter, *e.g.*, glycerin, alcohol, sugar, fats and oils, with ammonia, ammonium salts and alkaloids

**Antidotes.** Empty stomach by stomach tube. Give medicinal charcoal, stirred up in water. Keep patient lying down and warm. Strychnine,  $\frac{1}{2}$  gr., hypodermically. Calcium bromide intravenously or calcium gluconate intramuscularly has been recommended.

*Uses.* Solutions are strongly bactericidal and as a disinfectant its colour is an advantage. Even 1 in 1000 is efficient. It is a good deodoriser owing to its oxidising action and a 1% solution is useful in bromidrosis, also used as a dusting powder such as

potassium permanganate 13, alum 1, talc 50, zinc oxide 18, zinc chloride 18.

For gonorrhœa 1 in 10,000 to 1 in 1000 is used as a warm irrigation or injection. In ozœna a spray of 5 m. of 1% solution with 5 gr. of sodium chloride in 1 oz. of water is often effective.

As a gargle, mouthwash, or vaginal injection 1 of potassium permanganate in 5000 of water is useful. The solution is very nauseous to the taste. It may also be applied to foul ulcers and patches of gangrene, and to carbuncles as mild caustic. Internally it has been given in amenorrhœa in doses of 1 to 2 gr. as a pill 3 or 4 times daily before the expected period. 1 or 2 grains in a glass of soda water taken on an empty stomach is a certain cure for offensive breath.

Vomiting of pregnancy has been treated by 2 to 4 gr. of potassium permanganate in a cachet, giving immediately afterwards 3 to 4 oz. of water. Patient keeps this in the stomach 10 to 20 minutes—lying very still—then a pint or more of warm water. If necessary a further 1 g of permanganate per hour.

The crystals have been used to treat snake bite, the part being squeezed to remove the venom then the area around incised and the crystals rubbed in. A solution injected locally around the site has been used in the treatment of scorpion stings. A few crystals applied in a fold of lint will cause coagulation of the blood and stop hæmorrhage from superficial wounds of serous surfaces.

A fatal case of poisoning in a young man following injection into the urethra of a solution of 25 g of the crystals in a teacupful of water. Other fatalities have been recorded following ingestion of 15 to 20 g of the crystals—S G Willmott and M. Freeman, *Brit. med. J.*, 1/1936, 58.

ANTIDOTAL ACTION is distinct but limited even fairly dilute solutions are irritant, and a large dose may cause death. Potassium permanganate may be given orally in concentrations varying from 1 2000 to 1 5000, and 1 5000 may be used for washing the stomach, in poisoning by aconitine, amidopyrine, morphine, phenazone, picROTOXIN, and strychnine. It will not destroy all the poison, and its use should be followed by evacuation of the stomach. It is useless as an antidote in poisoning by atropine, cocaine, phosphorus, and by most of the synthetic hypnotics. There is no justification for the intravenous, subcutaneous, or intramuscular injection of potassium permanganate for the destruction of any poison in the circulation.—R A. Hatcher, *J. Amer. med. Ass.*, 11/1935, 502.

DERMATITIS among painters, following use of paint solvents, cured in 10 days by 1 : 1000 solution of potassium permanganate—J A Turner, per *Prescriber*, 1926, 351.

DYSENTERY, ASYLUM. A solution of permanganate, 1 gr. in 20 oz. is used. The patient swallows  $\frac{1}{2}$  to 1 or 2 oz. several times a day. In urgent cases, 20 m. approx. injected deeply into the buttocks—results often remarkable.—W. J. A. Erskine, *Brit. med. J.*, 1/1925, 530.

EPIDERMOPHYTOSIS, INTERTRIGO, ECZEMA MARGINATUM and eczematoid ringworm well treated by solution 1 in 5000 gradually increased—S Feldman and B. F. Ochs, per *J. trop. Med. (Hyg.)*, 1923, 198.

PYODERMIA well treated with baths containing potassium permanganate, copper or zinc sulphate, or sublimate.—*Brit. med. J. Epit.*, 11/1925, 80.

SMALLPOX. Potassium permanganate in saturated solution (5%) useful for painting the body. If skin sensitive, use 1 5%. In confluent cases patient put in a bath of this 5% solution, at body temperature, for 10 minutes. Reduces smell and sloughing.—*Lancet*, 11/1922, 1193.

VARICELLA treated by potassium permanganate baths, 5 to 6 g. for an adult or half the amount for children.—*Brit. med. J. Epit.*, 11/1925, 80.

**VENEREAL PROPHYLAXIS.** The immediate application of a solution of permanganate 1 in 1000 will prevent the occurrence of venereal disease—H Wansey Bayley, *Brit med J.*, 1/1921, 33 Its evils.—*ibid*, 66

### Thyroid and Manganese Treatment.

**ACUTE INFECTIONS, JOINT DISEASES, HEART DISEASE, ABNORMAL BLOOD PRESSURE, DISEASES OF PREGNANCY, DISORDERS OF METABOLISM, DIGESTIVE TROUBLES, NERVE COMPLAINTS, PULMONARY DISEASES, DISEASES OF THE SKIN, GOITRE AND MYXEDEMA, DISEASE OF THE BREAST, ETC.,** treated by rectal injections of potassium permanganate 1 gr in  $1\frac{1}{2}$  pints of sterile warm water. The amount is varied according to case, e.g., 2 doses of  $\frac{1}{2}$  pint may be found more effective than 1 dose of  $\frac{1}{2}$  pint. Warn patients they may feel some pain in the epigastrium within a few minutes, also they may pass long white skins or strings of mucus in the stools. Thyroid is given simultaneously—1 gr. twice daily, but doses of 6 gr or 5 or 10 gr. are in some cases desirable. Sometimes the permanganate may be used *per os*, in cachet, followed by a large draught of water, but this is not so good.—H. W. Nott, *Brit. med. J.*, 1/1925, 443; 11/1925, 1209

**PNEUMONIA.** Remarkable results. It is suggested that permanganate may be a specific. Treatment consists in rectal injections of 3 to 10 ounces of a potassium permanganate solution (4 grains in 3 pints) every 2 or 4 hours—H. W. Nott, *Brit med. J.*, 11/1926, 109 Basic principles underlying the treatment.—H W Nott, *Brit med J.*, 1/1928, 94 See also *Brit. med J. Ept.*, 11/1929, 43

Value of treatment confirmed in 5 consecutive cases of acute pneumonia—N J Roche, *Brit. med. J.*, 1/1927, 459 See also *Brit med J.*, 1/1927, 539.

A 1 in 7000 solution per rectum 4-hourly of value, even in debilitated children almost moribund; in conjunction with antipneumococcus vaccine a good armamentarium—A A. Hearne, *Brit med. J.*, 1/1928, 159. H L McCormick, *ibid.*, 377

Manganese and Thyroid "The most sure, the most scientific, the easiest treatment of all forms of cold or influenza."—F. A Hort, *Brit med J.*, 1/1933, 250

### Gargarisma Potassii Permanganatis (B.P.C.). 0.025% w/v.

**Injectio Potassii Permanganatis (L.H.)** has 5 grains in 1 pint, i.e. about 1 in 1600 C H W. has 1 in 1000 solution 4 dr, water to 2 pints, i.e. about 1 in 80,000.

**Liquor Potassii Permanganatis (B.P.C.)** Dose—2 to 4 drachms (8 to 15 ml). 1% w/v.

**Pilula Potassii Permanganatis.** 1, 2, 3, 4 or 5 grains with kaolin ointment, q s. **Caution!** Avoid mixing with any easily oxidised substance, like sugar, glycerin, etc. The pills may be coated with sandarac solution.

**Solvellæ Potassii Permanganatis** contain 5 gr. (0.3 g.).

**Calcii Permanganas.**  $\text{Ca}(\text{MnO}_4)_2 \cdot 5\text{H}_2\text{O} = 368.0$

Dose.— $\frac{1}{2}$  to  $1\frac{1}{2}$  grains (0.03 to 0.1 g.) in pills or capsules (with liquid paraffin as vehicle) thrice daily one hour before meals.

Deliquescent crimson crystals preferred for making mouth lotions, as it has less taste than the potassium salt. 1 in 100,000 sterilises water in 5 minutes; more powerful than the latter.

**Uses.** Similar to the potassium salt. Has been given in rodent ulcer, gastric ulcer and gastritis.

**Sodii Permanganas.**  $\text{Na}_2\text{Mn}_2\text{O}_8 = 283.9$ .

In solution, red in colour, is used as a cheap disinfectant. **Condy's Red Fluid** (Condy & Mitchell, London; *Pharmaceutical Products, London*) is stated to be a mixture of the sulphate and permanganate of soda—H R. Kenwood, *Lancet*, 1/1926, 1055 **Condy's Green Fluid** has sodium manganate,  $\text{Na}_2\text{MnO}_4 = 164.9$ , in solution.

**Zinci Permanganas (B.P.C.).**  $\text{ZnMn}_2\text{O}_8 \cdot 6\text{H}_2\text{O} = 411.3$ 

Brownish-black deliquescent crystals soluble 1 in 3 of water (usually leaving some residue). It is more readily reduced than the potassium compound. For lotions and injections, 1 gr. in 8 oz. (1 in 4000), where the astringent action of the zinc is indicated. As an eye wash 1 in 1000 to 1 in 2000. For pyorrhœa alveolaris and oral sepsis as mouth wash it is very useful.

**Caution.** Is liable to explode spontaneously and if the stopper of a bottle containing it becomes stuck, the bottle should be wrapped in a cloth before removal is attempted.

**Zinc permanganate bougies,** 4 inches long, containing  $\frac{1}{2}$  grain (0.03 g.) in oil of theobroma basis, are prepared.

**Inject. Zinc Permang.** (N.I.F.). Zinc permanganate 4 gr., water to 12 oz. To be diluted with an equal quantity of hot water (1 in 2625 when diluted). L.H. has  $\frac{1}{2}$  gr. in 3 oz. of water.

**Colloidal Manganese.** A colloidal solution of manganese hydroxide may be prepared by double decomposition of manganese chloride and sodium hydroxide, using dextrose as protective. Supplied in two separate solutions, each containing 0.5% of phenol.

The sodium chloride content is 0.53%. For use, mix equal quantities of the two solutions.

**Uses.** Gonorrhœa and sequelæ, also eczema, acne, quinsy and furunculosis have been treated by it.

HODGKIN'S DISEASE well treated after sodium cacodylate had failed to improve. —R. Samut, *Lancet*, i/1922, 17.

PSORIASIS treated—6 to 16 intramuscular injections —J. Moore, *Brit. med. J.*, ii/1922, 41. Urticaria treated —*Brit. med. J.*, ii/1923, 563.

**Collosol Manganese** (*British Colloids, London*) is supplied in two solutions, to be mixed at the time of use, producing a 0.25% solution. Also supplied ready mixed in ampoule form. **Collosol Manganese (Oral).** *Dose.*—A teaspoonful two or three times daily alone or in water.

In middle ear affections, internal nasal carbuncle, severe carbuncle on face, and erysipelas

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## MENTHOL

*B.P., U.S.P. XI, P. Helv. V, P. Dan*

$\text{CH}_3 \cdot \text{C}_6\text{H}_4(\text{OH})\text{C}_3\text{H}_7 = 156.16.$

*Syn.* *l-p*-MENTHAN-3-OL, METHYL-PROPYL-PHENOL-HEXAHYDRIDE.

*Dose.*— $\frac{1}{2}$  to 2 grains (0.03 to 0.12 g.), or more, in a pill with powdered soap, or in solution in olive oil.

A white crystalline substance obtained from the volatile oils of various species of *Mentha*. *B.P. Add.* recognises also lævo-rotatory synthetic menthol. *M.p.* 42° to 44°. *U.S.P. XI* also allows synthetic menthol.

**Soluble** 5 in 1 of alcohol 90%, 2 in 1 of ether, approximately 4 in 1 of chloroform, 1 in 4 of olive oil, 10 in 7 of light petroleum, and 1 in 6 of liquid paraffin. Freely soluble in essential oils, sparingly soluble in water, insoluble in glycerin. Soluble on warming in a strong solution of sodium salicylate, but thrown out again.

**Caution.** It is dangerous to apply an ointment containing menthol to the nostrils of infants, *e.g.*, for treatment of catarrh—it may cause instant collapse. *Cf.* Camphor.

**Uses.** Given internally, it is carminative and is occasionally given in the vomiting of pregnancy and other forms. Applied to the skin, it dilates the vessels, causing a sensation of coldness, and is useful for headache, rheumatic pains and neuralgia. For these purposes menthol cones are employed. It has antiseptic and anæsthetic properties, and gives great relief in prurigo, urticaria and pruritus ani. It liquefies when gently rubbed on the painful part.

As an antineuralgic in toothache and for sciatica 1 in 60 of alcohol with a little clove oil is employed. The crystals on cotton wool may be placed in the hollow of an aching tooth.

Menthol liquefies with an equal amount of either phenol, chloral hydrate or thymol, also 3 parts of menthol and 2 parts of camphor, 2 parts of menthol and 1 part of butylchloral hydrate, and 2 parts of menthol, with 1 each of phenol and butylchloral hydrate. These will relieve toothache. Its camphor and phenol combinations are used to medicate dry inhalers, and are most beneficial for arresting and curing colds, and relieving influenza and chest affections. Preparations of menthol are valuable for medicating hot moist air inhalations.

Menthol, camphor and other combinations, diluted with a heavy mineral oil, for spraying into the nares or in spirituous solution, inhaled as above, relieve swelling and irritability of nasal catarrh, contract capillary blood-vessels of mucous membrane, reduce swelling, relieve pain and fullness of head, arrest sneezing, and check excessive discharge.

In doses of 7½ grains, dissolved in olive oil in gelatin capsules, every 2 hours of value early in influenza. Reduces temperature in 18 to 24 hours, relieves pain, prevents post-influenzal debility, and lessens incidence of complications. —F. Schnapek, per *Brit. med. J. Epit.*, 11/1933, 61.

#### **Aqua Mentholis (B.P.C.)**

**Dose** —½ to 1 ounce (15 to 30 ml.). A saturated aqueous solution (about 1 in 1000).

**Emplastrum Mentholis (B.P.C.).** 15% in a basis of yellow wax and colophony. Useful for rheumatism and intercostal neuralgia.

**Gossypium Mentholis.** 10% Saturate cotton wool 85 with menthol 10 and liquid paraffin 5 in ether 265 and spread out to dry. Useful to plug the nose in nasal catarrh.

#### **Injectio Mentholis.**

Menthol 0.5, liquid paraffin 100. For use with a eustachian catheter to the middle ear.

**Insufflatio Mentholis (B.P.C.).** *Syn.* INSUFFLATIO MENTHOLIS COMPOSITA, MENTHOL SNUFF. Menthol 5% in ammonium chloride, boric acid and lycopodium. Relieves nasal catarrh.

[D.P. 81] **Insufflatio Mentholis et Cocainæ (B.P.C.).** Menthol 2½%, and cocaine hydrochloride 0.14% (½ gr per oz.) with ammonium chloride, camphor and lycopodium.



**[P1] Linimentum Mentholis.**

Menthol 3, chloroform 4, olive oil *q s.* to 16. Useful in lumbago, neuralgia, sciatica, and ringworm.

**Mentholeate.** Menthol and oleic acid *p æquales*. Heat gently to dissolve. Useful in pruritus, etc., where absorption is desired.

**Menthol-Paraffin Capsules** contain a 1% solution of menthol in liquid paraffin. These have elongated ends which can be torn off and the contents dropped into the ear to relieve earache.

**[P2] Menthophenol.** Menthol 3, phenol 1. Useful as gargle; 15 drops to the tumbler of water.

**Nebula Mentholis**, 0.5 to 2% in light liquid paraffin or olive oil is used for spray or pigment for throat. Relieves acute laryngitis.

**Nebula Mentholis Composita.** Menthol and camphor, 20 gr. each, cinnamon oil 5 m., light liquid paraffin to 1 oz.

**Nebula Mentholis et Thymolis Composita (B.P.C.).** Menthol, camphor and phenol, of each 2% *w/v*, with thymol, in light liquid paraffin.

**Neb. Menthol. c. Thymol. (N.I.F.).** Menthol 4 gr., thymol 2 gr., eucalyptol 2 m., light liquid paraffin to 1 oz.

**Pastilli Mentholis (B.P.C.)** contain  $\frac{1}{20}$  gr. (0.005 g.).

**[P1] Pastilli Mentholis et Cocainæ (B.P.C.)** contain menthol  $\frac{1}{20}$  gr. and cocaine hydrochloride  $\frac{1}{40}$  gr.

**Pigmentum Mentholis.** Menthol 1, olive oil 4. Painted or injected into the larynx, or even the trachea, is useful in phthisis and laryngeal disease. Also applied on wool for ear affections.

A solution of menthol 60 gr. in liquid paraffin or olive oil to 1 oz. is known in some clinics as "Pigmentum Melbæ," and is a great favourite with professional singers.—D. McKenzie, *Practitioner*, 11/1935, 663.

**Pigmentum Mentholis cum Guaiacol.** Menthol 1 gr., guaiacol in crystals 1 gr., oil of almond to 1 oz. Is often of value in acute tonsillitis.

**Pigmentum Mentholis et Tolueni (B.P.C.).** *Syn.* LÖFFLER'S PAINT. Menthol 10% *w/v*, with dehydrated alcohol, strong solution of ferric chloride and toluene. For diphtheria; to be applied on wadding every 3 hours. Painful in use; dilute hydrogen peroxide is preferable.

**Pilula Mentholis.**  $\frac{1}{2}$  to 2 grains. Mass with powdered soap or half its weight of white wax previously just melted.

**[D P1-81] Pulvis Mentholis et Cocainæ Compositus.** *Syn.* POUDRE CONTRE LE CORYZA (*Fr. Cx. Supp.*, 1920).

Menthol 1, cocaine hydrochloride 0.5, bismuth salicylate 45, boric acid 50.5.

**Spiritus Mentholis (B.P.C.).** 1 in 20.

**Spiritus Mentholis Compositus (B.P.C.).**

*Dose.*—10 drops, by inhalation. Camphor, menthol, terebene and eucalyptol, of each 1 in 10, in alcohol 90%.

**Tabellæ Mentholis.** *Dose.*—1 or 2.

Contain  $\frac{1}{2}$  gr. of menthol combined with chocolate.

**[P1] Tinctura Mentholis Ætherea.**

Menthol 1, ether 4 and chloroform 4. For local application in neuralgia.

**Unguentum Mentholis et Camphoræ.** Menthol 3% and camphor 2% in white soft paraffin. To be applied to the nasal passages in small quantity for hay fever.

**Vapor Mentholis Citriodoratus.**

Menthol, oil of *Eucalyptus Citriodora*, Cologne spirit and alcohol 90%, of each, equal parts.

A little inhaled, e.g., from an oro-nasal inhaler or the handkerchief, is valuable for nasal catarrh and influenza

### **Menthylis Valerianas.**

*Dose.*—10 to 15 minims (0.6 to 1 ml.).

A colourless liquid with agreeable odour and free from the burning taste of menthol. Nerve sedative. Used in sea-sickness.

**Valldol** (*Zimmer, Mannheim, Pharmaceutical Products, London*) is a mixture of menthol and menthyl valerianate. Available as liquid or in perles

## **MORPHINA**

*B.P.C., Fr. Cx., F.E. VIII.*



[D] "*Morphine and its salts, the esters of morphine and their respective salts*"

"Any solution or dilution of morphine or its salts in an inert substance, whether liquid or solid, containing any proportion of morphine, and any preparation, admixture, extract or other substance (not being such a solution or dilution as aforesaid) containing not less than one-fifth per cent of morphine."

[P1] "*Alkaloids, the following; their salts, simple or complex:—Morphine.*"

[S1] "*Alkaloids, the following; their salts, simple or complex:—Morphine except substances containing less than 0.2% of morphine calculated as anhydrous morphine*"

NOTE.—The esters do not include and should not be confused with the ethers of morphine, e.g., methyl-morphine (codeine) and ethyl-morphine (dionin)

*Dose* — $\frac{1}{8}$  to  $\frac{1}{2}$  grain (0.008 to 0.02 g.).

This, the principal alkaloid of opium, occurs as a white powder, or white, shining crystals. 3 parts of morphine are reckoned approximately equal to 4 parts of the acetate, hydrochloride or sulphate.

**Soluble** about 1 in 5000 of water, 1 in 100 of alcohol 90%, 1 in 4000 of chloroform, 1 in 3250 of benzene; almost insoluble in ether. 1 in 125 of glycerin, 1 in 10 of oleic acid; solutions of its salts are precipitated by ammonia and by potassium hydroxide (but redissolve in the latter).

Solubility at 20° is 1 in 6700 of water, 1 in 410 of alcohol 60%, 1 in 300 of alcohol 90%, 1 in 38 of dehydrated alcohol, 1 in 900 of alcohol-free pure chloroform or 1 in 500 of commercial chloroform containing alcohol.—H. Baggesgaard-Rasmussen and F. Reimers, *Dansk. Tidsskr. Farm.*, 1931, 5, 145.

**Incompatibility.** Morphine salts are decomposed by alkalis, and solutions are precipitated by vegetable compounds containing tannin. Also incompatible with iron, lead, manganese, silver, copper, and zinc salts and potassium permanganate.

The alkalinity of glass bottles may throw out a very appreciable amount of morphine from a solution of a salt.

**Antidotes.** Emetics would probably not act, so empty stomach by stomach tube, using 60 gr. of potassium permanganate in 2 gallons of water, and repeating the lavage frequently for a period of some hours. Stomach washing should be carried out even if the morphine has been taken hypodermically, because it seems to be excreted partly into the stomach. Keep the patient warm; rouse him by constant attention, flap him with a wet towel but do not walk him about. Give hot black coffee by mouth and by rectum, and medicinal charcoal, stirred up in water, freely. Atropine is the physiological antidote, and may be given hypodermically,  $\frac{1}{100}$  gr., or as tincture of belladonna. Strychnine,  $\frac{1}{8}$  gr., or caffeine sodium benzoate, 2 gr., hypodermically; Coramine, 5 to 15 ml. of 25% solution, intravenously. Artificial respiration and inhalations of oxygen with 7% carbon dioxide may be necessary. Urine must be drawn off with a catheter frequently.

**Morphine poisoning** in a baby of 10 days (due to pre-anæsthetic injection of  $\frac{1}{8}$  gr. morphine) combated by a mixture of 10% carbon dioxide and 90% oxygen. This mixture is known in the U.S.A. as 10-90.—J. R. McCurdy, *J. Amer. med. Ass.*, i/1929, 1927

**Treatment of Drug Addiction.** Morphine addicts are defined as persons who, not requiring the continued use of a drug for relief of symptoms of organic disease, have acquired, as a result of repeated administration, an overpowering desire for its continuance, and in whom withdrawal of the drug leads to definite symptoms of mental or physical distress or disorder.—From Departmental Committee Report on Morphine and Heroin Addiction, 1926, *Brit. med. J.*, i/1926, 814.

**Gradual Reduction Treatment** in the U.S.A. lasts about two months—

*During the first 20 days* the amount of morphine hypodermically is decreased gradually, and the decrease made up either by giving the deficit, plus 25%, by the mouth, or by exactly replacing the amount of morphine stopped with codeine sulphate. A gradually increasing dose of strychnine, either with the injection or *per os*, should be given.

*The next 8 to 12 days* should see the codeine entirely replace the morphine hypodermically, the strychnine as previously should be given and the morphine *per os* should be gradually diminished, though, of course, the volumes of all solutions given must remain the same. The daily amount of codeine must now be lessened, a period of about 10 to 20 days being occupied (according to the honesty and disposition of the patient) in reducing the amount to zero. During these last stages a bitter tonic should be given and a daily dose of hyoscine hydrobromide of  $\frac{1}{8}$  gr. is required.

Acidosis should be treated with magnesia, and cascara is useful for the frequently attendant constipation—E. H. Williams, "Opiate Addiction" (MacMillan, 1922).

**The Lambert-Towns Rapid Withdrawal Method** is an extraordinary one, in which enormous quantities of blue pill are given, together with decreasing amounts of morphine and increasing quantities of belladonna, xanthoxylum and hyoscyamus mixture, v. p. 273. The treatment appears to culminate in the administration of 2 ounces of castor oil, the nervousness of the patient being controlled with codeine.

**The Pettey Method** (George E. Pettey) includes the administration of hyoscine in  $\frac{1}{2}$  gr. doses, sparteine sulphate in 2 gr. doses and sodium thio-sulphate in doses of 20 gr. every 2 hours for 24 hours. Cathartic capsules containing calomel, cascara, ipecacuanha, strychnine and atropine are also given.

In these more rapid methods ethylmorphine is stated to be more efficacious than codeine; as it is about twice as powerful it is argued that half the dosage will suffice. This is taken advantage of in the following—

**Sceleth's Method**, in which ethylmorphine  $\frac{1}{2}$  gr. is combined with hyoscine, pilocarpine and cascara, and an amount varying with the amount of morphine taken is administered daily for 10 days. Then strychnine  $\frac{3}{16}$  gr., 3 times a day for 1 day, and on the following day the dose is halved and continued for a week. In about 4% of the cases hyoscine delirium has been observed. In such cases it should be omitted for a few doses.

Hyoscine and pilocarpine constitute the bases of **Bishop's Method** with sometimes the addition of heroin during the active stage.

In a typical case taking 12 gr. of morphine daily the dosage is cut down by 1 gr. daily until 6 gr. is reached, and this dose is continued until final reduction stage begins, when it is reduced by gradually decreasing amounts until final withdrawal 17 days later. Use a solution of 1 gr. in 30 m. and give 4 injections in 24 hours, at 8 a.m., 12 noon, 5 p.m. and 10 p.m. The bulk and appearance of the injection must always be the same and patient must never have any idea of the size of dose. During the initial stages (up to 6 gr.) both health and mental condition improve, but in the later stages and on total withdrawal there is great mental distress, insomnia, weakness, loss of appetite, and other symptoms. Blood pressure should be carefully watched: at withdrawal point the pulse becomes thready and this becomes more marked for 48 hours after withdrawal. If necessary, the injection of  $\frac{1}{2}$  gr. of morphine will restore pulse in a few minutes. During the final stage the patient is given the following mixture: Ammonium bromide 2 dr., potassium bromide 1 dr., tincture of kola 1 oz., concentrated compound infusion of gentian 1 oz., liquid extract of liquorice 4 dr., water to 6 oz. 1 teaspoonful every 2 hours in a little water, continued until 4 days after withdrawal and then for 6 to 8 weeks without the bromides. Also add  $\frac{3}{16}$  gr. of strychnine sulphate to the 8 a.m. injection, and inject 1 ml. of isotonic colloidal gold twice daily and  $\frac{1}{2}$  ml. calcium glycerophosphate, 3 gr. in 1 ml., once daily. Hot baths of value for restlessness. Alcohol should never be given either during or after withdrawal. Patient should be quite well and fit for work in from 4 to 6 months after withdrawal.—D. E. Stanford Park, *Practitioner*, 11/1927, 297. See also *ibid*, 1/1927, 56, and *Brit. med. J.*, 11/1927, 827, 1056.

Gradual and cautious withdrawal covered by two successive waves of over-dosage by "Special Mixture" (consisting of equal parts of tincture of belladonna and the fluid extracts of hyoscyamus and xanthoxylum, *cf.* p. 273), and Luminal respectively. When the total dose is reduced to  $\frac{1}{2}$  grain in 24 hours, without discomfort, for two days saline is given in place of the drug. No distress at any stage and no crisis. Treatment lasts ten to fourteen days.—G. Laughton Scott, *Practitioner*, 1/1927, 56.

A 0.1% solution of quinine hydrochloride gives the same bitter taste as a 0.5% solution of morphine, and may be substituted for it without the patient's knowledge.—H. Alpers, *Munch. med. Wschr.*, 1935, 1327.

**Intensive Treatment of Morphine Addiction.** Rapid relief from the craving for the drug in a simplified, painless and non-hazardous manner without the usual discomfort of withdrawal. The patient is first assured that permanent relief from the habit is possible, and that he will receive absolutely no more morphine when the treatment is started. Owing to the increased psychomotor activity during the intensive phase of the treatment, constant nursing service is required. Saline catharsis 5 drachms (19 g.) of Carlsbad salt for one or two doses precedes treatment. Scopolamine and pilocarpine are given hypodermically as follows—(1) Scopolamine hydrobromide  $\frac{1}{160}$  gr., 1 dose; (2) scopolamine hydrobromide  $\frac{1}{160}$  gr., 5 doses, 1 every hour; (3) scopolamine hydrobromide  $\frac{1}{160}$  gr., 21 doses, every 2 hours; (4) pilocarpine nitrate  $\frac{1}{2}$  gr. 2 hours after the last dose of scopolamine and continued for a total of 5 doses, 1 every hour. Every patient treated has stated that he did not recall what had taken place during the treatment, had not experienced any physical or mental distress whatever, and had no desire for morphine. After the intensive treatment (48 hours) the following powder is given and continued for 6 to 8 weeks to restore the blood calcium level, which falls during the administration of sedatives and hypnotic drugs:—Scopolamine hydrobromide  $\frac{1}{2}$  gr., calcium phosphate compound (magnesium phosphate 2, dibasic calcium phosphate 8, calcium glycerophosphate 8, potassium bicarbonate 32, sodium bicarbonate to 100) 2 drachms, divided into 24 doses, 1 capsule being taken 3 times a day before meals. Of 57 patients treated 55% were permanently relieved and 12% relapsed.—T. Klingmann and W. H. Everts, *J. Amer. med. Ass.*, 1/1936, 18.

**Auto-serotherapy.** Blistering the patient and reinjecting the blister fluid, from two to five injections being given. The patient no longer needs or desires the drug. Remarkably good results in Egypt—M Vivian, *Lancet*, ii/1934, 273

**THE TREATMENT OF DRUG ADDICTION.** an exhaustive review of modern withdrawal methods—"abrupt," "rapid," and "gradual"—with a bibliography of 57 references—E. W. Adams, *Practitioner*, ii/1932, 234, 390

**Uses of Morphine Salts.** A general and most useful sedative and anodyne for all purposes, preferably hypodermically, but may cause indigestion and constipation. Is of particular value in sleeplessness due to pain, acute fevers or heart disease. In mania and epilepsy other narcotics acting also on the motor cells are preferred. Small doses are frequently effective in controlling uræmic convulsions, but some consider morphine to be contra-indicated in renal disease. Is of value in preventing useless cough, but must not be used when there is much secretion. For the production of "twilight sleep" morphine is used in conjunction with hyoscine (*q.v.*). As a pre-operative sedative, morphine is now largely replaced by the basal narcotics. Hæmoptysis is well treated by  $\frac{1}{4}$  to  $\frac{1}{2}$  gr hypodermically.

**CARDIAC ASTHMA,** acute attacks. Morphine  $\frac{1}{2}$  grain subcutaneously of great value.—Claude Wilson, *Lancet*, ii/1923, 1346

**CORONARY THROMBOSIS.** Violent substernal pain treated by  $\frac{1}{4}$  gr of morphine and  $\frac{1}{32}$  gr. of hyoscine—as salts—failed to yield, but  $\frac{1}{4}$  gr of morphine intravenously gave dramatic effect. It is not known whether morphine salts intravenously are safe, but it was effective in this case—F Moor, *Lancet*, ii/1930, 959.

**IN LABOUR** morphine lessens the frequency of contractions, but pains pass off more slowly, so that the work done by the uterus is probably as great as or greater than before, despite lessened frequency—A W. Bourne and J H Burn, *Brit. med. J.*, ii/1930, 87

**WHOOPIING COUGH** cured by small doses of morphine more speedily than by any other remedy.—*Brit. med. J.*, i/1925, 1007.

Morphine acts only on certain pain centres in the brain, and is therefore wasted in lead and opium lotion and laudanum fomentations. Rectal morphine suppositories are efficacious only so far as morphine is absorbed and carried to the brain. We are apt to fear the secondary effects of morphine too much, rather than too little, and to forget that large doses of the synthetic products may cause sweating, rashes, and sometimes cyanosis—E B Leech, *Lancet*, i/1924, 915

May be given without fear of renal complications secondary to its use—R. S. Ackley, *J. Amer. med. Ass.*, i/1930, 79, *Lancet*, i/1930, 364

[D P1 81] **Oleatum Morphinæ.** Morphine 1, oleic acid 60. Dissolve

Oleic acid will dissolve as much as one-tenth of its weight of pure morphine. Morphine is added to oleate of mercury to relieve pain

[D P1 81] **Morphinæ Acetas (B.P.C.).**

$C_{17}H_{19}O_3N, C_2H_4O_2, 3H_2O = 399.2$

**Dose.**— $\frac{1}{8}$  to  $\frac{1}{2}$  grain (0.008 to 0.02 g.), which may be increased.

A white powder with faintly acetous odour. Soluble 1 in  $2\frac{1}{2}$  of water, about 1 in 100 of alcohol 90%, and 1 in 5 of glycerin.

[P1] **Linctus Morphinæ Hydrocyanicus** (Ogle's Drops) (*St. G H.*)

Dilute hydrocyanic acid 1 m., solution of morphine acetate 3 m., oxymel of squill to 1 dr.

[D-P1 81] **Liquor Morphinæ Acetatis (B.P.C.)**

**Dose.**—5 to 30 minims (0.3 to 2 ml.). 1%.

[D-P1-81] **Pastillus Morphinæ Acetatis** ( $\frac{3}{8}$  gr.).

[D-P1 81] **Pastillus Cocainæ** ( $\frac{1}{8}$  gr) et **Morphinæ** ( $\frac{1}{8}$  gr)

**[D P I 81] Morphinae Hydrobromidum.**

$C_{17}H_{19}O_3N \cdot HBr \cdot 2H_2O = 402.1$ .

*Dose.*— $\frac{1}{8}$  to  $\frac{1}{2}$  grain (0.008 to 0.03 g.).

A white powder, soluble 1 in 22 of water and about 1 in 50 of alcohol 90%. Given with hydrobromic acid as sedative.

**[D P I 81] Morphinae Hydrochloridum (B.P., Fr. Cx., P.G. VI, P. Helv. V, P. Dan., P. Ital. V, F.E. VIII, P. Belg. IV)**  
 $C_{17}H_{19}O_3N \cdot HCl \cdot 3H_2O = 375.7$ .

*Dose.*— $\frac{1}{8}$  to  $\frac{1}{2}$  grain (0.008 to 0.02 g.), which may be increased.

In silky white crystals or in powder. Soluble 1 in 25 of water, about 1 in 50 of alcohol 90%, and about 1 in 8 of glycerin; insoluble in ether or chloroform.

**[D P I 81] Guttæ Morphinae et Cocainæ (Aural).** Morphine hydrochloride 4 gr., cocaine hydrochloride 24 gr., glycerin 1 drachm, distilled water to  $\frac{1}{2}$  oz.  
*N.B.* A potent preparation

**[D P I 81] Injectio Morphinae (B.P.C.)**

*Dose*—5 to 10 minims (0.3 to 0.6 g.)

Contains 2½% of morphine hydrochloride (about  $\frac{1}{4}$  gr. in 10 m.)

**[D P I 81] Soluté de Morphine chlorhydrate pour injection hypodermique (Fr. Cx.)** is 2% Solutio Morphini Hydrochloridi (P. Stec. X) is 3%.

**[P I] Linctus Morphinae (U.C.H.)**

Solution of morphine hydrochloride 3 m., emulsion of chloroform 3 m., treacle 60 gr., water to 1 dr. May be more agreeably flavoured with syrup of lemon

*Dose*—A teaspoonful 3 or 4 times a day, repeated frequently when cough is troublesome. Taken undiluted, swallowed very slowly. For children of 8 to 14 years, dose 10 to 20 drops. Not suitable for very young children or in difficulty of expectoration in bronchitis

**[P I] St. M. H.** has solution of morphine hydrochloride 10 m., honey  $\frac{1}{2}$  dr., water to 1 dr.

**[P I] Linct. Morph. Rub. (N.I.F.)** (chloroform  $\frac{1}{2}$  m., solution of morphine hydrochloride 5 m., vinegar of ipecacuanha 10 m., vinegar of squill 10 m., solution of bordeaux B  $\frac{1}{2}$  m., syrup of Virginian prune to 1 dr.

**[D P I 81] Liquor Morphinae Hydrochloridi (B.P.).**

*Dose.*—5 to 30 minims (0.3 to 2 ml.) 30 m. contains about  $\frac{1}{4}$  gr. of morphine hydrochloride.

Morphine hydrochloride 1, dilute hydrochloric acid 2, alcohol 90% 25, distilled water to 100.

**[P I] Mistura Morphinae et Phenazoni Composita.**

*Dose.*—1 ounce (30 ml.)

Solution of morphine hydrochloride 10 m., phenazone 10 gr., tincture of castor 20 m., spirit of chloroform 10 m., Syl. Lavandulæ 1 dr., mucilage q.s. water to 1 oz.

This is virtually a specific for spasmodic dysmenorrhœa

**[P I] Mist. Tuss. Rub. (N.I.F.). Syn. Mist. Tuss. Acid.**

Solution of morphine hydrochloride 5 m., vinegar of ipecacuanha (B.P. '98), 10 m., syrup of squill 30 m., solution of bordeaux B 2½ m., chloroform water to  $\frac{1}{2}$  oz.

**[D-P I 81] Suppositorium Morphinae (B.P.).** Unless otherwise stated contains  $\frac{1}{4}$  grain (0.015 g.) of morphine hydrochloride in oil of theobroma q.s. to 15 grains

**[D P I 81] Tablets, Hypodermic,** contain  $\frac{1}{8}$ ,  $\frac{1}{4}$  and 1 grain. Also morphine hydrochloride  $\frac{1}{4}$  gr., atropine sulphate  $\frac{1}{250}$  gr. and glyceryl trinitrate  $\frac{1}{250}$  gr., for use in asthma

[P1] **Trochisci Chlorodyni** (B.P.C.) contain  $\frac{1}{80}$  gr. of morphine hydrochloride (equivalent to about 8 m. of tincture of chloroform and morphine).

[P1] **Trochisci Morphinae** (B.P.C.) contain  $\frac{1}{80}$  gr. of morphine hydrochloride.

[P1] **Trochiscus Morphinae et Ipecacuanhae** (B.P.)

Contains  $\frac{1}{80}$  grain (0.002 g.) of morphine hydrochloride, with  $\frac{1}{80}$  grain (0.006 g.) of powdered ipecacuanha. Useful to allay cough.

[D P1-81] **Morphinae Meconas.** *Syn.* MORPHINE BIMECONATE.  
( $C_{17}H_{19}O_5N$ )<sub>2</sub>.C<sub>7</sub>H<sub>4</sub>O<sub>7</sub>.5H<sub>2</sub>O = 860.4.

*Dose.*— $\frac{1}{8}$  to  $\frac{1}{2}$  grain (0.008 to 0.03 g.)

This, one of the natural salts of morphine in opium, is in white minute acicular crystals, soluble 1 in 34 of water. It is said to disturb the head and the stomach less than the other salts.

[D P1 81] **Liquor Morphinae Bimeconatis.**

*Dose.*—5 to 40 minims (0.3 to 2.4 ml.)

Morphine 14 $\frac{1}{2}$  gr., meconic acid 12 gr., alcohol (90%) 1 oz., mix and add distilled water to 4 oz. Filter. 1 ounce contains about 6.3 gr. or 1.45% (w/v) of morphine meconate. It is about the same strength as tincture of opium.

[D P1 81] **Morphinae Sulphas** (B.P.C., U.S.P. XI).

( $C_{17}H_{19}O_5N$ )<sub>2</sub>.H<sub>2</sub>SO<sub>4</sub>.5H<sub>2</sub>O = 758.5

*Dose.*— $\frac{1}{8}$  to  $\frac{1}{2}$  grain (0.008 to 0.02 g.)

In white, silky acicular crystals. Soluble 1 in 21 of water, very slightly in alcohol 90% (about 1 in 700).

[D-P1-81] **Hypodermic Tablets** contain  $\frac{1}{8}$ ,  $\frac{1}{4}$ ,  $\frac{1}{2}$ ,  $\frac{3}{4}$ ,  $1$  and  $1$  grain; also combined with atropine as follows:—

{ Morphine sulphate  $\frac{1}{8}$ ,  $\frac{1}{4}$ ,  $\frac{1}{2}$ ,  $\frac{3}{4}$ ,  $1$  gr. }  
{ Atropine sulphate  $\frac{1}{80}$ ,  $\frac{1}{40}$ ,  $\frac{1}{20}$ ,  $\frac{1}{10}$ ,  $\frac{1}{5}$  gr. }

Morphine and atropine are given before anaesthesia, effected by gas and ether, to lessen the amount required and to minimise the secretion from the mouth and lungs.

[D-P1-81] **Steriles Morphine Sulphate** (Martindale, London). Ampoules containing  $\frac{1}{2}$  or  $\frac{1}{4}$  gr. of morphine sulphate in 1 ml. of 50% w/v magnesium sulphate solution for production of analgesia in childbirth (see p. 139).

[D P1 81] **Morphinae Tartras** (B.P.).

( $C_{17}H_{19}O_5N$ )<sub>2</sub>.C<sub>4</sub>H<sub>6</sub>O<sub>6</sub>.3H<sub>2</sub>O = 774.4

*Dose.*— $\frac{1}{8}$  to  $\frac{1}{2}$  grain (0.008 to 0.02 g.)

In small white nodular tufts of acicular crystals, readily soluble 1 in 11 of water, slightly in alcohol 90%, insoluble in ether or chloroform.

[D P1 81] **Liquor Morphinae Tartratis** (B.P.C.).

*Dose.*—5 to 30 minims (0.3 to 2 ml.). 1%.

[P1 81] **Æthylmorphinae Hydrochloridum** (B.P.C., P. Hung., P. Svec., P. Jap. IV, Fr. Cx. Supp. 1926, U.S.P. XI, P.G. VI, P. Ned. V, P. Belg. IV, P. Helv. V, P. Dan., P. Ital. V). *Prop. Name.* DIONIN (Merck, Darmstadt; Martindale, London).  
C<sub>17</sub>H<sub>23</sub>O<sub>3</sub>N.HCl.2H<sub>2</sub>O = 385.7.

[P1] "*Alkaloids, the following, their salts, simple or complex:—Ethylmorphine.*"

[81] "*Alkaloids, the following, their salts, simple or complex:—Ethylmorphine, except substances containing less than 0.2% of ethylmorphine*"

NOTE—Although ethylmorphine and its salts are controlled by the *Methylmorphine and Ethylmorphine Regulations, 1933*, these regulations do not affect any sale or distribution of the drugs by any person other than a wholesaler or any sale or distribution by an authorised seller of poisons in the course of any retail business (see page 1034)

*Dose.*— $\frac{1}{16}$  to  $\frac{1}{2}$  grain (0.006 to 0.03 g.), by the mouth;  $\frac{1}{4}$  to  $\frac{1}{2}$  grain (0.0025 to 0.008 g.), by hypodermic injection *Fr. Cx. Supp.* 1926 has max dose in 24 hours 3 grains (0.2 g.), *P.G. VI* 5 grains (0.3 g.).

A white crystalline powder, m.p. about  $123^{\circ}$ , obtained by the action of diethyl sulphate on morphine in alkaline alcoholic solution and recrystallisation from hydrochloric acid (see *Edn. XIX*, p. 565). Morphine contains one phenolic and one alcoholic group. In ethylmorphine the H of the phenolic group is replaced by  $C_2H_5$ .

*Soluble* about 1 in 10 of water, 1 in 25 of alcohol 90%; insoluble in ether and chloroform

*Uses.* To replace codeine and morphine in bronchitis, pulmonary emphysema and bronchial asthma, and for whooping-cough.

A useful anodyne in glaucoma, iritis, corneal ulcers, etc., and is of service in interstitial keratitis with potassium iodide internally and yellow precipitate ointment in the conjunctival sac. Solutions may be from 1 to 5% strength or more, but it may cause "ophthalmic fireworks," pain, chemosis, swelling and sneezing.

CORNEAL OPACITIES 5% ethylmorphine hydrochloride solution, provided a good reaction is set up, seems useful—*T. L. de Courcy, Brit med J.*, ii/1921, 737

[P1 81] *Elixir Æthylmorphinæ et Terpini (B.P.C.)*

*Dose.*— $\frac{1}{2}$  to 1 drachm (2 to 4 ml.).

Contains  $\frac{1}{2}$  gr. of ethylmorphine hydrochloride and  $\frac{1}{8}$  gr. of terpin hydrate in alcohol 90%, glycerin and syrup of wild cherry to 1 drachm.

[P1 81] *Guttæ Ethylmorphinæ Hydrochloridi (R.L.O.H.) Syn. GUTTÆ DIONINÆ*

Contain 4, 8, 20 or 40 gr. of ethylmorphine hydrochloride in 1 oz. of sterilised water.

**Diamorphinæ Hydrochloridum (B.P.).**

$C_{21}H_{23}O_5N, HCl, H_2O = 423.7$ . *Syn. and Prop. Name.* DIACETYLMORPHINE HYDROCHLORIDE (*P.G. VI, P. Helv. V, P. Dan., Fr. Cx. Supp.* 1926, *P. Jap. IV*), HEROIN HYDROCHLORIDE (*Bayer Products, London*).



[D] "*Diacetylmorphine and its salts, any preparation, admixture, extract or other substance containing any proportion of diacetylmorphine.*"

[P1] and [S1] "*Alkaloids, the following, their salts, simple or complex.—Diacetylmorphine.*"

Several countries are now prohibiting or discouraging the use of heroin. Spain prohibits the prescription and dispensing of any medicine containing it, and so does Costa Rica. In Paraguay, though the use of heroin is not forbidden, it is subject to the strictest possible control, while in the United States its employment is apparently being actively discouraged—Report of Advisory Committee of the League of Nations on Traffic in Opium and other Dangerous Drugs, *Summary of Annual Repts for 1933*

*Dose* — $\frac{1}{4}$  to  $\frac{1}{2}$  grain (0.0025 to 0.008 g) *P G VI, P Helv V* and *P Dan* have max in 24 hours approx  $\frac{1}{2}$  grain *Fr. Supp.* 1926,  $\frac{1}{2}$  grain.

A colourless crystalline powder, m.p. 229° to 233°, obtained by the action of acetic anhydride on morphine. The hydrogen atoms of both the alcoholic and phenolic OH groups are replaced by the CH<sub>3</sub> CO group

**Soluble** about 1 in 2 of water and about 1 in 11 of alcohol 90%

**Incompatibles.** Both alkalis and acids and other chemicals as morphine.

**Antidotes.** Treat as for poisoning by morphine, see p. 638.

Recovery after 9 grains is on record

**Heroin and Morphine Addiction.** Heroin is used sometimes by injection and sometimes as a snuff like cocaine. The addict prefers it to morphine. The morphine addict has only one or two stools a week, whereas the bowels of the diamorphine addict are almost normal. There is not so much pallor or emaciation.—W. E. Dixon, *Brit med J.*, ii/1921, 821

**Addicts in Egypt** prefer their diamorphine intravenously—believed to be due to the rapid relief obtained from intravenous injection of drugs for bilharzia. Terrible results follow its use—A. G. Biggam, *Trans R. Soc. trop. Med. Hyg.*, ii/1929, 147

Egypt has roughly half a million drug addicts. Drugs taken for sexual stimulation, in ignorance of the fact that they are a common cause of impotence—J. D. Rolleston, per *Med Annu*, 1931, 14.

Of 200 addicts in Egypt, 138 used heroin, 20 opium, 14 hashish, 12 morphine, 8 manzöl (a mixture of hashish, dry spices and herbs), 6 mixtures and 2 cocaine. Owing to the transmission of malaria in 1929 the intravenous route fell into disrepute, and heroin is now usually taken by snuffing, the average dose being 1 to 2 gr daily. Description of a 7-day special substitution treatment employing morphine, phenobarbitone, intramuscular magnesium sulphate and paraldehyde.—A. G. Biggam and co-workers, *Lancet*, i/1932, 923

Addicts in Egypt now reduced to 150,000. Heroin no longer imported in bulk. Estimated there are 282,000 hashish addicts. Under Egyptian legislation traffickers of foreign nationality cannot be proceeded against, otherwise the illicit traffic in that country would be very largely reduced—*Lancet*, i/1932, 1372.

Whereas in 1932 the number of heroin, cocaine, opium and hashish addicts in Egypt were 5695, 714, 7141 and 18,871 respectively, in 1934, as a result of the work of the Egyptian Central Narcotics Intelligence Bureau, the figures were reduced to 1605, 279, 5237, and 11,552 respectively, or a reduction of from 0.23 of the total population to 0.133.—E. W. Adams, *Bull Hyg*, 1936, 341.

**Uses.** Sedative for cough, *e.g.* in phthisis, bronchitis, and laryngitis, also in asthma. Has been given in hæmoptysis. Lengthy use must be guarded against. Useful in acute coryza.

Often more effectual than morphine in relief of severe nerve pain. It does not constipate. The danger of addiction from its continual use must never be forgotten.

Although diamorphine (hypodermically) is preferable to morphine for relief of pain after abdominal operations, care should be taken to see that the patient is *fully roused from the anæsthetic before administering*, and only  $\frac{1}{2}$  gr. should be given, repeated if necessary, as the effect of larger doses may be very dangerous to the respiratory centre. Artificial respiration necessary in two cases—A. E. M. Woolf, *Brit. med. J.*, 1/1929, 499, see also *ibid*, 975.

[D P1 S1] **Elixir Diamorphinæ et Pini Compositum** (B P C).

*Dose.*— $\frac{1}{2}$  to 1 drachm (2 to 4 ml.).

Contains about  $\frac{1}{16}$  gr. of diamorphine hydrochloride,  $\frac{5}{16}$  gr. of terpin hydrate and  $\frac{1}{2}$  m. of oil of pumilio pine in 1 dr.

[D P1 S1] **Elixir Diamorphinæ et Terpini** (B P C)

*Dose*— $\frac{1}{2}$  to 1 drachm.

Contains about  $\frac{1}{16}$  gr. of diamorphine hydrochloride and  $\frac{5}{16}$  gr. of terpin hydrate in a syrup of wild cherry menstruum.

[P1 S1] **Elixir Diamorphinæ et Terpini cum Apomorphina** (B.P.C.).

*Dose.*— $\frac{1}{2}$  to 1 drachm (2 to 4 ml.) diluted.

Contains  $\frac{1}{16}$  gr. of diamorphine hydrochloride and  $\frac{1}{16}$  gr. of apomorphine hydrochloride, with  $\frac{5}{16}$  gr. of terpin hydrate in 1 dr. (*exempt* [D]).

[D-P1 S1] **Glycerinum Diamorphinæ** (B.P.C.).

*Dose*— $\frac{1}{2}$  to 2 drachms (2 to 8 ml.).

Contains about  $\frac{1}{16}$  gr. of diamorphine hydrochloride in 1 drachm with acid infusion of roses in a water-alcohol-glycerin menstruum.

[D P1 S1] **Linctus Diamorphinæ** (B.P.C.).

*Dose*— $\frac{1}{2}$  to 2 drachms (2 to 8 ml.).

Contains about  $\frac{1}{16}$  gr. of diamorphine hydrochloride in 1 dr., with tincture of hyoscyamus, syrup of wild cherry, syrup of tolu and glycerin.

[P1 S1] **Linctus Diamorphinæ Camphoratus** (B P C)

*Dose*— $\frac{1}{2}$  to 1 drachm (2 to 4 ml.)

Contains  $\frac{1}{16}$  gr. of diamorphine hydrochloride in 1 dr., with small doses of squill and ipecacuanha (*exempt* [D]).

[P1 S1] **Linctus Diamorphinæ cum Ipecacuanha** (B P.C)

*Dose.*— $\frac{1}{2}$  to 1 drachm (2 to 4 ml.).

Contains  $\frac{1}{16}$  gr. of diamorphine hydrochloride in 1 dr., with a little ipecacuanha, hyoscyamus and tolu (*exempt* [D]).

[P1 S1] **Linctus Diamorphinæ et Scillæ** (B P.C.).

*Dose.*— $\frac{1}{2}$  to 1 drachm (2 to 4 ml.).

Contains  $\frac{1}{16}$  gr. of diamorphine hydrochloride in 1 dr., with  $\frac{1}{16}$  gr. of sodium antimonyltartrate and a little squill and senega (*exempt* [D]).

[P1-81] **Linctus Diamorphinæ et Thymi (B.P.C.).**

*Dose.*— $\frac{1}{4}$  to 1 drachm (2 to 4 ml.).

Contains  $\frac{1}{10}$  gr. of diamorphine hydrochloride in 1 dr. and  $\frac{1}{2}$  gr. of apomorphine hydrochloride, with liquid extract of thyme, tolu and glycerin (*exempt* [D])

[D-P1-81] **Pastilli Diamorphinæ Hydrochloridi** contain  $\frac{1}{10}$  gr (0.0016 g.).

[D-P1-81] **Pastilli Diamorphinæ et Pini Compositi (B.P.C.)** contain  $\frac{1}{4}$  gr. of diamorphine hydrochloride,  $\frac{1}{4}$  m. of oil of pumilio pine and  $\frac{1}{8}$  gr. of terpin hydrate.

[D-P1-81] **Morphine Methylbromide.** *Syn.* MORPHOSAN  
 $C_{17}H_{19}O_2NBr \cdot H_2O = 398.1$

*Dose.*—*Hypodermically*,  $\frac{1}{4}$  to  $\frac{1}{2}$  grain (0.008 to 0.016 g.)

White needles soluble 1 in 20 Compared with morphine it is non-poisonous—it is thought to be 10 times less potent.

*Uses.* In epilepsy, also for use with hyoscine *q.v.* as anæsthetic

[D-P1-81] **Morphine Methylchloride**,  $C_{17}H_{19}O_2NCl \cdot 2H_2O = 389.7$ , is a similar compound, soluble 1 in 10 of water

The hydrochloride of this base is readily soluble 1 in 200, the sulphate 1 in 170—D. B. Dott, *Pharm J.*, 1/1926, 356

[D-P1-81] **Benzylmorphinæ Hydrochloridum.**

$C_{17}H_{19}O_2N(OCH_2C_6H_5) \cdot HCl = 411.7$ . *Prop. Name* PERONIN  
 (Merck, Darmstadt; Martindale, London).

[D] *Benzylmorphine and its salts; any preparation, admixture, extract or other substance containing any proportion of benzylmorphine or its salts.*

[P1] and [81] "*Alkaloids, the following, their salts, simple or complex:—Benzylmorphine*"

*Dose.*— $\frac{1}{8}$  to  $\frac{1}{4}$  grain (0.008 to 0.03 g.).

Colourless microcrystalline powder with bitter taste.

**Soluble** 1 in 200 of water, 1 in 160 of alcohol 90%; insoluble in chloroform and ether. Similar in therapeutic properties to codeine and ethylmorphine and administered with expectorants for local irritation of respiratory organs

[D-P1-81] **Morphine Narcotine Meconate.** *Prop. Name* NARCOPHIN (P.G. VI) (Boehringer, Mannheim, not available in Gt Britain)

*Dose*— $\frac{1}{4}$  to  $\frac{1}{2}$  grain (0.02 to 0.03 g.)

Yellowish crystals containing about 30% of morphine and 43% of narcotine, soluble 1 in 5 of water approximately, but not completely

*Uses.* Hypnotic It is similar in action to morphine and hyoscine, and is used where morphine is employed, also where morphine alone is inadmissible (diseases of organs of respiration, etc.).

It is stated that the paralyzing action of morphine on the respiratory centre is lessened greatly by adding an equal quantity of narcotine. In the case of mice the toxicity of the two together is so small as to be hardly measurable The greatest increase in narcotic effect is obtained by using equal weights

[P1-81] **Papaverina (B.P.C., F.E. VIII).**  $C_{20}H_{21}O_4N = 339.2$

[P1] "*Alkaloids, the following; their salts, simple or complex — Papaverine.*"

[81] "*Alkaloids, the following; their salts, simple or complex:—Papaverine, except substances containing less than 1% of papaverine.*"

*Dose*—2 to 4 grains (0·12 to 0·25 g.) An alkaloid of opium (0·5 to 1%) M.p. 147°. Easily soluble in hot alcohol, but with difficulty in cold.

[P 181] **Papaverinæ Hydrochloridum** (*P. Helv V, P. Dan, P. G. VI, P. Ned. V, P. Svec. X, P. Belg IV, F.E. VIII, P. Ital V*)  $C_{20}H_{21}O_4N \cdot HCl = 375.6$ .

*Dose*—2 to 4 grains (0·12 to 0·25 g.). *P. Helv V* has max. single dose approx. 3 grains, max. in 24 hours 10 grains, by hypodermic injection  $\frac{1}{2}$  and  $2\frac{1}{2}$  grains respectively

A white crystalline powder slowly soluble 1 in 40 of water, giving an acid solution. Is used for the same purposes as the sulphate.

[P 181] **Papaverinæ Sulphas.**  $(C_{20}H_{21}O_4N)_2 \cdot H_2SO_4 = 776.4$

*Dose*.—2 to 4 grains (0·12 to 0·25 g.). *per os* or hypodermically, up to 8 grains (0·5 g.) in a day

A white crystalline powder soluble 1 in 2 of water. It is said to be non-toxic in single doses of even 1 g.

A rather feeble central analgesic and a local anæsthetic. Does not induce a habit like morphine. In all kinds of gastric and intestinal spasms (also for the diagnosis of pyloric spasm), in biliary colic and in bronchial spasm. Of more doubtful value in pertussis, hyperemesis and vascular spasm—angina pectoris, acute uræmia and eclampsia. The local anæsthetic action, with vasodilation, has been used against rhino-asthma, and to mitigate the pain of irritant injections. Ureteral calculi have been treated by instillation through a catheter of 5 ml. of 2% solution.

[P 181] **Tablets of Papaverine** (base)  $\frac{1}{2}$  gr., **Hyoscyamine** (base)  $\frac{3}{16}$  gr., and **Benzyl Succinate** 5 gr. have been employed for calmativ analgesic effect.

[D P 181] **Spasmalgin** (*Hoffmann-La Roche, London*) Combination of papaverine 0·02 g., Omnopon 0·01 g. and Atrial (a sulphonic derivative of atropine) 0·001 g. in tablet form, or in solution in ampoules. For pathological conditions due to spasm of plain muscle, e.g., gastric pain, cardiac asthma, dysmenorrhœa, hiccup, renal colic and sea-sickness. *Dose*—1 to 2 ampoules or tablets a day, increased to 4 in severe cases.

**Perparine.** A synthetic derivative of papaverine in which the four methoxy groups are replaced by four ethoxy groups. The action is stated to be similar to that of papaverine, but to be two or three times more intense with only one third the toxicity. Suggested as a morphine substitute in the treatment of conditions in which pain is produced by spasm of plain muscle. Biliary colic, cholecystitis, vesical spasm, renal calculus, asthma and dysmenorrhœa successfully treated. **Surparine**, a combination of Perparine and Novatropine (brom-methyl-homatropine), particularly efficacious.—M. G. Pouchet, *per Brit. med. J.*, 1/1934, 812.

**Eupaverin** (*Merck, Darmstadt, Martindale, London*). A synthetic compound,  $C_{18}H_{19}O_4N$ , with action similar to papaverine, but stated to be less toxic.

[P 181 84] **Eupaco** (*Merck, Darmstadt, Martindale, London*). Combination of Eupaverin, atropine methylbromide, diethylaminophenazone and phenylethyl-barbituric acid, in tablets or suppositories. For spastic conditions of smooth muscle and for obstetric cases when long and difficult labour is expected.

**Octon** (*Knoll, Ludwigshafen, Pharmaceutical Products, London*) Methyl-octenylamine, an unsaturated aliphatic base, supplied in the forms of its bitartrate (in tablets containing  $2\frac{1}{2}$  gr.) and hydrochloride (in 10% solution). In its paralyzing effect on the smooth musculature it is 5 to 10 times more active than papaverine and its effect is of longer duration; its toxicity is from  $1\frac{1}{2}$  to 2 times that of papaverine. *Dose*.—1 tablet or 15 to 20 drops of solution 3 times daily

Antispasmodic and anodyne in pain due to spasms. It is also supplied in ampoules of 1 l ml (1 ml contains  $1\frac{1}{2}$  gr of Octon hydrochloride) for subcutaneous or intramuscular injection.

[D P1 S1] **Thebaine Hydrochloride** (*P. Ned. V, P. Helv. V*).

$C_{19}H_{21}O_3N \cdot HCl, \frac{1}{2}H_2O = 356.6$ .

[D] "*Thebaine and its salts, any preparation, admixture, extract or other substance containing any proportion of thebaine or its salts*"

[P1] "*Alkaloids, the following, their salts, simple or complex.—Thebaine.*"

[S1] "*Alkaloids, the following, their salts, simple or complex — Thebaine, except substances containing less than 1% of thebaine*"

*Dose.*— $\frac{1}{10}$  to 1 grain per os increased with care, hypodermically  $\frac{1}{10}$  grain.

The salt of an alkaloid of opium, soluble about 1 in 15 of water. Has been used in neuralgic affections.

**Chelidonium Majus.** *Syn.* GREATER CELANDINE. The yellow milky juice is an old remedy for warts and opacities of the cornea. The freshly expressed juice preserved by  $\frac{1}{4}\%$  v/v of chloroform has been used as a remedy for cancer, given in dose of 10 to 60 minims, and in some cases with striking results. Internally it has an action similar to that of papaverine, and the powdered root has been used, in a dose of 15 to 30 grains, in the treatment of asthma, spasmodic colic and gastralgia. A fluid extract (*Dose*—10 to 30 minims) from the dried plant has been used for injection into diseased tissue, and, diluted, as a lotion. An alkaloid, chelidonine,  $C_{20}H_{19}NO_4 \cdot H_2O = 371.2$ , has been isolated, melting at  $135^\circ$ . The hydrochloride and a sulphate have been used as morphine substitutes.

## NARCOTINA

(with COTARNINA)

*B.P.C.*

$C_{19}H_{14}O_4N(OCH_3) = 413.2$ .

*Syn.* ANARCOTINE

*Dose.*—1 to 3 grains (0.06 to 0.2 g) or more in a pill

An alkaloid from opium (sometimes as much as 15% is present), in white crystals, insoluble in water, soluble 1 in 3 of chloroform, 1 in 100 of 90% alcohol, 1 in 125 of ether, soluble also in benzene. An anti-periodic of great power, analogous to quinine. Has been used in malaria and in sleeping sickness.

**Narcotine Hydrochloride** (*P. Ned. V, P. Helv. V, P. Dan*).

*Dose.*—1 to 3 grains (0.06 to 0.2 g). White crystals soluble about 1 in 4 of water.

**Narceina.**  $C_{19}H_{17}NO_3 \cdot 3H_2O = 499.3$ .

*Dose.*— $\frac{1}{2}$  to 1 grain. An opium alkaloid soluble in alcohol, almost insoluble in water. Hypnotic sedative of doubtful utility. **Narceine Hydrochloride** (*P. Ned. V, P. Helv. V*). Action is similar to morphine, but it is rarely used in medicine.

[P1 81] **Cotarninae Chloridum** (B P C.)

$C_{12}H_{15}O_3NCl \cdot 2H_2O = 291.6$ . *P. Helv V* has  $1\frac{1}{2}$  to 2  $H_2O$ . *Syn and Prop Names* COTARNINE HYDROCHLORIDE (*P. Ned. V, F E VIII, P G. VI, P. Helv V*), OKISTYPIN (*Richter, London*), STYPTARNIN (*Allen & Hanburys, London*), STYPTICIN (*Merck, Darmstadt; Martindale, London*)

[P1] "Alkaloids, the following, their salts, simple or complex — Cotarnine."

[81] "Alkaloids, the following, their salts, simple or complex — Cotarnine except substances containing less than 0.2% of cotarnine"

*Dose*.— $\frac{1}{4}$  to  $1\frac{1}{2}$  grains (0.02 to 0.1 g) internally or hypodermically in special cases up to 4 grains in 10% solution.

The salt of the base cotarnine, in primrose coloured, deliquescent granular crystals, very soluble in water and alcohol

[P1 81] **Cotarnine Phthalate**. *Prop Name*. STYPTOL (*Knoll, Ludwigshafen, Pharmaceutical Products, London*)

$(C_{12}H_{15}NO_4)_2 \cdot C_6H_4(COOH)_2 = 640.3$

*Dose*.— $\frac{3}{4}$  grain (0.05 g), but much larger doses are given by some practitioners, e.g., 10 grains, without unpleasant effects, every 2 to 3 hours.

A pale yellow crystalline powder, m.p.  $113^\circ$ , consisting of the acid phthalate. Soluble 1 in 60 of water. Contains 59% of cotarnine.

**Lodal** (*Burroughs Wellcome, London*) 6-7-Dimethoxy-2-methyl-3,4-dihydroisoquinolinium, an oxidation product of laudanose, in 1 gr tablets. For the control of uterine hæmorrhage. *Dose*.—1 or 2 tablets thrice daily

[P1 81] **Cotarnina**,  $C_{12}H_{15}O_4N$ , is obtained by oxidising narcotine with nitric acid. In colourless needles, m.p.  $132^\circ$  to  $135^\circ$ , sparingly soluble in water, soluble in alcohol and ether.

Cotarnine is generally regarded as anomalous in containing water which cannot be removed, while the dried hydrochloride is anhydrous. But if the latter is regarded as cotarnine chloride and the base as cotarnine hydroxide, there is nothing anomalous.—D. B. Dott, *Chem. & Drugg.*, 1/1932, 14

**Uses**. Given internally in all forms of uterine hæmorrhage, useful in checking profuse menstruation. 1 to 2% may be used locally on a tampon.

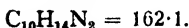
Erysipelas, eczema and shingles may be treated with a 5% ointment

A 2% ointment in a basis of wool-fat ointment is useful in herpes and ulcerative balanitis. In more acute similar complaints up to 10% strength can be employed.

[P1 81] **Urethral Bougies of Cotarnine** in cacao butter or gelatin contain  $\frac{1}{4}$  grain (0.03 g), 4 inches long, and  $\frac{1}{8}$  inch in diameter, are used to check bleeding caused by sounds or catheters

## NICOTINA

B.P.C



Syn. PYRIDYL-METHYL-PYRROLIDIN.

[P2] "Nicotine; its salts"

[S1] "Alkaloids, the following; their salts, simple or complex:—Nicotine."

[S3] "Alkaloids—Nicotine—in Tobacco."

A colourless, hygroscopic volatile liquid alkaloid (darkens in time) from tobacco, *Nicotiana Tabacum*. The content may be from 0.5 to 5%, combined as malate or citrate. Sp. gr. about 1.01.

**Antidotes.** Empty stomach by emetic, or by stomach tube using dilute tannic acid solution. Give 5 gr doses tannic acid, repeated if necessary, or medicinal charcoal in water, freely. Keep patient lying down and warm. Stimulants, e.g., brandy  $\frac{1}{2}$  oz. or aromatic spirit of ammonia  $\frac{1}{2}$  dr in water, strychnine  $\frac{1}{4}$  gr., or caffeine sodium benzoate 2 gr, hypodermically. Artificial respiration and oxygen inhalations may be necessary.

Nicotine poisoning is a temporary respiratory emergency comparable to drowning (or electrical shock) and should be treated as such. Experiments on dogs with nicotine poisoning treated by (a) artificial respiration alone, and (b) artificial respiration with intracardiac injection of adrenaline. Results quoted in detail. It is suggested that prolonged artificial respiration and, when the heart has stopped, intracardiac injection of adrenaline, should be tried in cases of acute nicotine poisoning in the human —Frank and Thomas, *J Amer med Ass*, 1/1936, 507.

The *Lancet* Laboratory conducted an enquiry into the toxic factor in tobacco. Pipe mixtures contained the largest amount of nicotine (2.04 to 2.85%), Egyptian, Turkish and Virginian cigarettes came next with 1.38 to 1.8%. A British cigar contained less (1.24%) and a Havana cigar least of all (0.64%). The cigarette (from any tobacco) yields least of its nicotine to the smoke, while the pipe yields a very large proportion, of its nicotine (70 to 80% in some cases) to the smoke reaching the mouth of the consumer. Cigarette smoke contains, however, furfural (a harmful substance), especially the cheap Virginian cigarettes —this is practically absent in the smoke both of the cigar and pipe. Further, the cigar, pipe and Egyptian and Turkish cigarettes all yield ammonia, which is an antidote to furfural and aldehydes generally. The cheap Virginian cigarettes contain very little ammonia.

Tobacco 100 g., as cigarettes, yields, when burnt in conditions approximating those which occur in smoking HCN 0.08 g, pyridine 0.146 g, nicotine 1.165 g, NH<sub>3</sub> 0.36 g., carbon monoxide 410 ml (No CO is produced in opium smoking).

Generally speaking, most of the nicotine in smoking is destroyed during combustion. Carbon monoxide poisoning liable to occur from cigarettes in excess. All the symptoms are in evidence in the man who smokes 20 cigarettes a day —Prof Dixon, *Brit med J.*, 11/1921, 819; *Lancet*, 11/1921, 1071.

Carbon monoxide in tobacco smoke. The amount varies according to rate of smoking. In general, a normal sample of cigarette smoke will contain between 0.5 and 1% of CO. A cubic foot of coal gas contains as much CO as 4 cigars. CO may apparently replace oxygen in the blood without serious harm. —Prof. H. E. Armstrong, *Brit. med. J.*, 1/1922, 992.

**Denicotinised Tobacco.** Physicians are warned not to recommend denicotinised tobaccos without further evidence than manufacturers' assurance, since in Germany some samples were found to have more than the normal content of nicotine —*Lancet*, 11/1925, 32.

German view of nicotine. German brands of so-called nicotine-free cigars gave upwards of 420 and 320 mg. per 100 g.—presumably in smoke. Nicotine deadly to adolescents —Prof. Klonka, *Lancet*, 1/1926, 563.

**Medical Aspects of Tobacco.** A "drug of addiction" only in a humorous sense but hardly accurate. Psychological tests on medical students show that smoking lowers mental efficiency in 10 to 23%, especially in imagery, perception and association. Effects on the heart described. Effect on athletics doubtful. The irritating effect on the throat ascribed variously to furfural, pyridine and ammonia—not to nicotine—Sir H. Rolleston, *Lancet*, 1/1926, 961

**The Effects of Tobacco Smoking.**

(a) On the digestive system.—Sir H. Rolleston; (b) From the nervous and mental aspect.—Sir R. Armstrong Jones, (c) The physiological effects.—Prof W. E. Dixon, *Practitioner*, 1/1927, 1. See also *Brit. med. J.*, 11/1927, 719

**Uses.** Is practically never used in medicine, but has been suggested for use in post-encephalitic parkinsonism. Nicotine is used as a horticultural insecticide either as vapour or as a spray. For vaporisation 1 oz. is sufficient for 2000 to 8000 cu. ft. As a spray  $\frac{1}{2}$  to 1 oz. of nicotine with  $\frac{1}{2}$  to 1 lb. of soft soap is used in 10 gallons of water

POST-ENCEPHALITIC PARKINSONISM treated by nicotine. Cases which may benefit are those where voluntary muscular control is intact, but movement is hampered by excessive plastic tone. Nicotine base is used. Signs of intolerance are nausea, fainting, tachypnoea, and are watched for. Patient is kept in bed. Initial dose  $\frac{1}{10}$  grain *ter die*. If no appreciable change in pulse chart the dose was increased to  $\frac{1}{5}$  or  $\frac{1}{4}$  grain *ter die*. Immediate results indisputable.—H. Moll, *Brit. med. J.*, 1/1928, 1079

[P2 81] **Nicotinæ Sulphas**,  $\frac{1}{4}$  grain, has also been given by injection in post-encephalitic conditions

[P2 81] **Nicotinæ Salicylas**.  $C_{10}H_{14}N_2 \cdot C_6H_4(OH)COOH = 300.3$ . White crystals freely soluble in water. 0.1% solution or ointment has been used in scabies

**Piperazina** (*B.P.C.*, *Fr. Cx.*, *F.E. VIII*)

$HN < \begin{smallmatrix} CH_2 & CH_2 \\ | & | \\ CH_2 & CH_2 \end{smallmatrix} > NH \cdot 6H_2O = 194.2$  *Syn* PIPERAZINE HYDRATE

*Dose*—5 to 15 grains (0.3 to 1 g.)

In colourless, glassy deliquescent tablets, absorbing atmospheric carbon dioxide to give the carbonate, and containing 44% of anhydrous piperazine. M.p. about 43°. M.p. of anhydrous base about 109°. Is obtained by the action of sodium glycol on ethylene-diamine hydrochloride (for details, see *Edn. XIX*, p. 702)

**Incompatible** with alkaloidal salts, iron salts, quinine, sodium salicylate, spirit of nitrous ether.

**Uses.** Given internally for the uric acid diathesis, in gout and rheumatism, and urinary calculi. Said to prevent change from glycogen into sugar in diabetes

**Piperazina Effervescens** (*B.P.C.*)

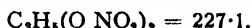
*Dose*—1 to 3 drachms (4 to 12 g.) Contains about 5 grains per drachm.

**Sidonal** (*Boehden, Berlin*) is piperazine quinate. **Sidonal, New** is said to be the anhydride of quinic acid. Both are used in gout and rheumatism.

**Urazine** (*Pharmaceutical Specialities (May & Baker) Ltd., London*) Piperazine citro-salicylate in effervescent granules and in tablets containing 0.3 g. for use in rheumatism, gout, etc



## NITROGLYCERINUM



*Syn.* TRINITROGLYCERIN, GLONIN, TRINITRIN, GLYCERYLIS TRINITRAS

[P1] "*Glyceryl trimtrate.*"

*Dose.*— $\frac{1}{100}$  to  $\frac{1}{50}$  grain (0.0003 to 0.0013 g) increased to  $\frac{1}{10}$  grain.

Tolerance may develop to a marked degree but is of exceeding short duration. A case recorded failing to respond after 6 months' use to 500 times the initial dose—H B Myers and V T. Austin, *J Pharmacol*, June, 1929, 227.

Nitroglycerin is a dense, opaque, white, oily liquid, transparent when dehydrated, and of sp. gr 1.600. It has no odour, is slightly volatile, and has a sweet, aromatic and pungent taste. It is slightly soluble in water, freely soluble in ether, 1 in 6 of almond oil, freely soluble in absolute alcohol, and 1 in 15 of 90% alcohol. Nitroglycerin in fatty or oily solution is perfectly safe and stable, but in alcoholic solution the substance must be handled with the utmost caution.—*Vide infra.*

**Incompatibility.** Nitroglycerin is decomposed by caustic alkalis. The alcoholic solution is also precipitated by water in excess.

**Antidotes.** Keep patient lying down and warm, apply ice to the head. Give 30 m of liquid extract of ergot by mouth, repeating the dose if necessary. Ephedrine hydrochloride,  $\frac{1}{4}$  gr. hypodermically, has been recommended. Artificial respiration may be necessary.

Strychnine, ergot and belladonna are recommended to counteract the headache produced by large doses.

**Uses.** Physiologically it has the action of the nitrites and is especially valuable in angina pectoris and in asthmatic paroxysms, also generally to relieve dyspnoea of cardiac, pulmonary or renal origin.

Nitroglycerin, within 2 minutes after taking, accelerates the pulse, dilates the arteries, produces a feeling of fullness all over the body, but particularly in the head by a throbbing at the sides of the temples. It also causes headache, which lasts from 15 minutes to several hours, according to the quantity taken; but to patients accustomed to its use the headache is not felt. In treating angina pectoris, neuralgia, asthma, headache, sea-sickness and Bright's disease, its action is like that of amyl nitrite and the other nitrites, but its effects last much longer. For the weak heart of fatty degeneration and of old persons, this lessened tension proves valuable. It has been given in hæmoptysis, and is of value in sea-sickness. Repeated doses can be given with perfect safety.

In tinnitus aurium has been found useful. A dose of any preparation of nitroglycerin acts more promptly if taken on an empty stomach. In arteriosclerosis patients are made more comfortable by small doses for a week or two.

**HÆMOPTYSIS.** The action of nitroglycerin on pulmonary circulation does not justify its use and, experimentally, it appears to be contraindicated in hæmoptysis—*Per J. Amer. med. Ass.*, 11/1925, 929

**HIGH BLOOD PRESSURE** Salines, exercise, sodium nitrite in 3 or even 5 gr. doses several times daily with a diuretic or diaphoretic. Amyl nitrite or nitroglycerin for temporary effect—should not be used too early—*J. Henderson, Glasg. med. J.*, Apr., 1923, 209

**High blood pressure** A trinitrin tablet, in some cases, helps patient to sleep.—*Sir H. Rolleston, Lancet*, 1/1923, 521.

**MIGRAINE** Over 80% of cases completely controlled by taking tablets of nitroglycerin (0.5 mg.) over a long period—half a tablet after breakfast, half after the midday meal, and in severe cases a third dose in the evening. Should be chewed, not swallowed whole.—*Dollken, Practitioner*, 1/1928, 334

**NEPHRITIS, ACUTE TUBULAR, ACCOMPANIED WITH DROPSY** Nitroglycerin is valuable as in the following—Trinitrin solution 32 m, potassium acetate 5 dr., compound cardamom tincture 4 dr., water to 8 oz. *Dose*— $\frac{1}{2}$  ounce in water every 3 hours, until symptoms abate, and then thrice daily. Iron tonics to be given so soon as the urine is albumin-free—*J. T. MacLachlan, Brit. med. J.*, 11/1923, 473

**SLA-SICKNESS** Recommended—*A. Sellheim, Brit. med. J.* 1/1928, 244.

**[P1] Haustus Nitroglycerini.**

Solution of glyceryl trinitrate 1 m, sodium bicarbonate 10 gr., compound tincture of cardamom 1 dr., spirit of chloroform 20 m, water to 1 $\frac{1}{2}$  oz. To be slowly sipped at first symptoms of an attack as restorative in angina pectoris

**[P1] Gowers' Migraine Mixture.** Sodium bromide 5 to 10 gr., solution of glyceryl trinitrate 2 m, dilute hydrobromic acid 5 m, tincture of nuxvomica 5 m, tincture of gelsemium 5 to 10 m, syrup of lemon 1 dr., water to  $\frac{1}{2}$  oz. To be taken three times a day after food. Tincture of belladonna 5 to 10 m can usefully be included either in addition to, or in place of, the nuxvomica. This mixture must be taken for long periods in severe cases, but not during an attack. It should be supplemented by phenobarbitone  $\frac{1}{2}$  gr. every night and when an attack threatens—*D. Brinton, Practitioner*, 1/1936, 528

**[P1] Injectio Nitroglycerini Hypodermica.**

*Dose*—1 to 4 minims (0.06 to 0.25 ml.)

Solution of glyceryl trinitrate 5, alcohol (90%) 2, distilled water to 12

Contains about  $\frac{1}{10}$  gr. in 1 m. Acts promptly and is useful in collapse, etc., when the patient cannot swallow

**[P1] Liquor Glycerylis Trinitratis (B.P., F.E. VIII, P. Hung., P.G. VI, P. Belg. IV, P. Helv. V, P. Ned. V) Syn. SOLUTIO NITROGLYCERINI SPIRITUOSA I.A., LIQUOR TRINITRINI, LIQUOR NITROGLYCERINI, SPIRITUS GLYCERYLIS NITRATIS**

*Dose*— $\frac{1}{2}$  to 2 minims (0.03 to 0.12 ml.). The dose may be increased gradually to 10 minims, if necessary, every 3 or 4 hours, in any aqueous vehicle. 2 minims contains about  $\frac{1}{10}$  gr. of glyceryl trinitrate

A 1% w/v solution of glyceryl trinitrate in alcohol 90%. *P. Ned. V* gives directions for making direct from glycerin by nitration with a mixture of nitric and sulphuric acids.

A colourless neutral liquid, 10 ml with an equal volume of water keeps clear, but diluted further, the glyceryl trinitrate separates in oily drops, which explode when struck with a hammer. Should be kept from sunlight. A 5% and a 10% solution in absolute alcohol are also prepared commercially but are not safe for use in dispensing. A little caustic potash solution should be poured over it to decompose should it be accidentally spilled. Headache may be caused by applying it freely to the skin.

[P1] **Spiritus Glycerylis Trinitratis** (U.S.P. XI).

*Average dose.*—1 minim (0.06 ml).

An alcoholic solution containing about 1% w/v of glyceryl trinitrate, and of the same strength therefore as the Liquor of the B.P.

[P1] **Tabella Glycerylis Trinitratis** (B.P.). *Syn.* TABELLÆ TRINITRINI, TABLETS OF NITROGLYCERIN.

Tablets of chocolate, each weighing 0.3 g. (5 grains), and containing 0.0005 g. ( $\frac{1}{200}$  grain).

*Dose.*—1 or 2 tablets.

Tablets are also available containing  $\frac{1}{30}$ ,  $\frac{1}{20}$ ,  $\frac{1}{10}$ ,  $\frac{1}{5}$ ,  $\frac{1}{2}$  and  $\frac{1}{15}$  grain.

[P1] **Tabellæ Glycerylis Trinitratis** (U.S.P. XI)

*Average dose.*— $\frac{1}{10}$  grain (0.0006 g.) of glyceryl trinitrate.

No definite weight or strength is prescribed for these tablets, but they are required to contain from 87.5 to 112.5% of the amount of glyceryl trinitrate stated on the label.

[P1] **Tabellæ Nitroglycerini Compositæ.**

Nitroglycerin  $\frac{1}{10}$  gr., amyl nitrite  $\frac{1}{2}$  gr., menthol  $\frac{1}{10}$  gr., capsicum  $\frac{1}{10}$  gr.

[P1] **Tabellæ Nitroglycerini et Caffeinæ.**

*Dose.*—1 every 4 hours or as required. Contain  $\frac{1}{10}$  gr of nitroglycerin and 1 gr. of caffeine, for use in migraine.

[P1 §1] **Tabellæ Nitroglycerini et Sodii Iodidi cum Arsenio.** *Dose*—1 in every 4 hours. Each equivalent to nitroglycerin  $\frac{1}{10}$  gr., sodium iodide 15 gr., with arsenical solution 2 m. This dosage may be considered a routine treatment of aortic disease. The quantity of nitroglycerin employed is frequently too low, but the above may be given with perfect safety.

[P1] **Tabellæ Anti-Asthmaticæ.** (H.)

*Dose.*—1 to 4 thrice daily.

Nitroglycerin  $\frac{1}{30}$  gr., sodium iodide 2 gr., potassium bromide 2 gr., liquid extract of euphorbia 3 m., tincture of lobelia 4 m.

Very useful in asthma, the nitroglycerin depresses the peripheral ends of the vagus nerve and stimulates the heart by removing the inhibitory action of the vagus and relieving blood vessels elsewhere.

[P1 §1] **Tabellæ Nitroglycerini**  $\frac{1}{10}$  gr. (0.0004 g.) **et Strychninæ**  $\frac{1}{2}$  gr. (0.0025 g.)

Also { nitroglycerin  $\frac{1}{30}$ ,  $\frac{1}{20}$ ,  $\frac{1}{10}$  grain with  
strychnine  $\frac{1}{30}$ ,  $\frac{1}{20}$ ,  $\frac{1}{10}$  grain

In migraine nitroglycerin, especially in combination with strychnine, is of value. It relieves headache almost immediately. Its vasodilator effect lowers blood pressure in the peripheral vessels, and so reduces cerebral and arterial pressure.

In high arterial tension where the heart is beginning to fail and such symptoms as irregularity of pulse, giddiness, shortness of breath, or even oedema of ankles begin to appear, Brunton advised to combine cardiac tonics with vasodilators. Rest is of utmost importance.

[P1] **Hypotensive Tablets** (Parke, Davis, London) contain lithium hippurate 2 gr., sodium nitrite 1 gr., nitroglycerin  $\frac{1}{30}$  gr. *Dose*—1 to 2 tablets. For the treatment of high blood pressure.

**Explosives.**

**Dynamite** consists of nitroglycerin absorbed on diatomite.

**Carbonite** consists of nitroglycerin 25, potassium nitrate 30, barium nitrate 4, wood meal 40, sodium carbonate 1.

**Cordite** is stated to contain nitroglycerin 30, nitrocellulose 65, soft paraffin 5. Other mixtures are known as **Gelignite** (containing 56.5%), **Samsonite** and **Saxonite**.

# NUX VOMICA

B.P., U.S.P. XI, P. Dan., P. Helv. V, F.E. VIII, P. Belg. IV,  
P. Ital. V

Syn. STRYCHNI SEMEN I.A.

[P1] "Nux Vomica."

"Alkaloids, the following, their salts, simple or complex:—  
Brucine; Strychnine"

[B1] "Nux Vomica, except substances containing less than 0.2% of  
strychnine."

"Alkaloids, the following, their salts, simple or complex:—  
Brucine, except substances containing less than 0.2% of brucine;  
strychnine, except substances containing less than 0.2% of  
strychnine"

Dose.—U.S.P. XI has average dose  $1\frac{1}{2}$  grains (0.1 g.). The  
B.P. requires that when Nux Vomica is prescribed, Nux Vomica  
Pulverata shall be dispensed

The dried ripe seeds of *Strychnos Nux-Vomica* (Loganiaceæ),  
imported from India and Ceylon, containing not less than 1.2%  
of strychnine U.S.P. XI requires not less than 1.15% of  
strychnine

I.A. (Second) recommended a standard of 2.5% of total alka-  
loids Fr. Cx requires not less than 2%, nor more than 3%  
of (combined) alkaloids

**Antidotes.** Treat as for poisoning by strychnine, see p. 866.

**Uses.** A bitter stomachic and tonic. Stimulates the bowels,  
hence added to aperients. Increases nervous energy. Given as a  
cardiac and respiratory stimulant in collapse. Is employed in  
dyspepsia, heart weakness, and as a general tonic in all conditions  
of debility and neurasthenia. For the aged, this and strychnine  
have been described as the only suitable bitter tonics

In phosphaturia, small doses of nux vomica and dilute hydro-  
chloric acid are often of great service—Tirard, *Med. Treatment*.

[P1 B1] **Extractum Nucis Vomicae Siccum** (B.P.) Syn. Ex-  
TRACTUM NUCIS VOMICÆ

Dose.— $\frac{1}{4}$  to 1 grain (0.016 to 0.06 g.)

Contains 5% of strychnine, adjusted with calcium phosphate;  
1 grain contains about  $\frac{1}{4}$  grain of strychnine.

Fr. Cx conforms with I.A. (Second) making the preparation  
16% of total alkaloids, with max. single dose  $\frac{1}{2}$  grain and max. in  
24 hours  $1\frac{1}{2}$  grains approx. Elsewhere abroad the extract is called  
Extractum Strychni. P.G. VI, P. Ital. V, F.E. VIII and P. Belg.  
IV also agree with I.A. (Second)

[P1 B1] **Extractum Nucis Vomicae** (U.S.P. XI)

Average dose.— $\frac{1}{4}$  grain (0.015 g.)

Contains 7.4% of strychnine, and is therefore 50% stronger than  
the dry extract of the B.P.

[P1 81] **Extractum Nucis Vomicae Liquidum (B.P.).**

*Dose.*—1 to 3 minims (0.06 to 0.2 ml.).

Prepared by percolating the seeds in powder with alcohol 70%, defatting with hard paraffin, and adjusting the strength so that the extract contains 1.5% *w/v* of strychnine. 3 minims contains about  $\frac{1}{12}$  grain. *P. Ital. V* has 2.5% of alkaloids.

[P1 81] **Nux Vomica Pulverata (B.P.)** *Syn* PULVIS NUCIS VOMICÆ.

*Dose.*—1 to 4 grains (0.06 to 0.25 g.). 4 grains contains about  $\frac{1}{6}$  grain of strychnine.

Nux vomica in fine powder adjusted by admixture with stronger or weaker nux vomica, or with lactose, to contain 1.2% of strychnine.

[P1] **Tinctura Nucis Vomicae (B.P.)**

*Dose.*—10 to 30 minims (0.6 to 2 ml.), often less

Liquid extract of nux vomica 8.34% *v/v*, with alcohol 90% and distilled water. It contains 0.125% *w/v* of strychnine; 30 minims contains about  $\frac{1}{10}$  grain.

*I.A. (Second)* recommended 0.25% of total alkaloids. *P. Belg IV, F.E. VIII* and *P. Ital. V* conform to this standard.

*Fr. Cx* prepares by dissolving 1.562 g. of extract (*Fr. Cx*) in alcohol 70% *q.s.* to produce 100 g. This contains 0.25% of combined alkaloids (*I.A.*). Max single dose, 19 minims; max during 24 hours, 95 minims approximately.

**PSYCHONEUROSIS.** Most sufferers from functional nervous illness are considerably benefited by a mixture such as the following, which is best styled a sedative tonic sodium bromide 5 gr., tincture of nux vomica 5 to 10 m., spirit of chloroform 10 m., compound infusion of gentian to  $\frac{1}{2}$  oz. *Dose*— $\frac{1}{2}$  oz. thrice daily, after meals.—*D. Brinton, Practitioner*, 1/1936, 524.

[P1] **Tinctura Nucis Vomicae (U.S.P. XI).**

*Average dose.*—15 minims (1 ml.).

Prepared by maceration with a mixture of hydrochloric acid, alcohol and water, followed by percolation with a diluted alcohol and adjusting the volume to contain 0.114% *w/v* of strychnine, the tincture is then cooled to 5° for  $\frac{1}{2}$  hour and filtered.

[P1 81] **Ignatia (B.P.C.).** *Syn.* ST. IGNATIUS BEAN.

*Dose.*— $\frac{1}{2}$  to 2 grains (0.03 to 0.12 g.)

The dried ripe seeds of *Strychnos Ignatu* (Loganiaceæ), containing strychnine and brucine, the alkaloidal content being 2.5 to 3%, of which rather more than half is strychnine.

**Antidotes.** Treat as for poisoning by strychnine, *see* p. 866

[P1] **Tinctura Ignatiæ (B.P.C.).**

*Dose.*—5 to 20 minims (0.3 to 1.2 ml.) 1 in 10.

[P1 81] **Teinture de Fève de Saint-Ignace Composée (Fr Cx)** *Syn* GOUTTES AMERES DE BAUMÉ.

*Dose.*—Max. single 4 minims, max during 24 hours 30 m., approximately

Prepared by macerating 1 of ignatia, 0.025 of potassium carbonate and 0.05 of purified wood tar in 5 of alcohol 70%

[P1 81] **Cabalonga de Tabasco (P. Mex V)** Mata-perros, Veneno del diablo. The seeds of *Strychnos triplinervia*. According to Professor Graham, they contain 1.83% of strychnine and brucine. Used in place of ignatia.

**Damiana** (*B.P.C.*). *Syn.* TURNER, HYSTERIONICA, BAYLAHUEN.

The dried leaves of *Turnera diffusa* var. *aphrodisiaca* (Turneraceæ) and probably other species. Contains a bitter principle, damianin, resins and  $\frac{1}{2}$  to 1% of volatile oil. Is laxative and tonic, and has aphrodisiac properties.

**Extractum Damianæ** (*B.P.C.*)

*Dose.*—5 to 10 grains (0.3 to 0.6 g). A soft extract.

**Extractum Damianæ Liquidum** (*B.P.C.*).

*Dose.*— $\frac{1}{2}$  to 1 drachm (2 to 4 ml). 1 in 1.

[P1] **Mistura Damianæ Compositum** (*B.P.C.*)

*Dose.*—1 to 2 drachms (4 to 8 ml.)

Contains  $\frac{1}{2}$  dr. of liquid extract of damiana, 2 m. of liquid extract of nux vomica and calcium and sodium hypophosphites in chloroform water to 2 dr.

[P1 81] **Pilulæ Damianæ Compositæ** (*B.P.C.*)

*Dose.*—1 pill.

Contain extract of damiana 2 gr, phosphorated suet  $\frac{1}{10}$  gr, and dry extract of nux vomica  $\frac{1}{10}$  gr.

## OCULENTA

All ointments for the eye should be made with the official basis of wool fat 10, soft paraffin 90, in accordance with the directions of the *British Pharmacopœia*, unless otherwise ordered. If the medicament is readily soluble in water it should be dissolved in the smallest quantity of sterilised water. This solution should then be incorporated in the melted sterilised basis, and the mixture triturated continuously until cold. If the medicament is not readily soluble in water it should be finely powdered, thoroughly levigated with a small quantity of the basis and finally incorporated with the remainder.

The ointment should be packed in a sterilised container and stored in a cool place. Small collapsible tubes with special tapering ends are very suitable containers, since there is a much smaller risk of contamination than when a pot is used. The tubes are best filled by inverting them in cold water and pouring in the ointment, previously softened by carefully heating after the manner used for moulding suppositories. Sterilised soft gelatin capsules are also used as containers. This latter method of packing has the advantage that sufficient ointment for one dose may be placed in each capsule.

When the medicament is in the form of an aqueous solution of an alkaloidal salt emulsified in the basis, the action is exerted much more rapidly and is more powerful than when it is in the form of an alkaloid in solution or suspension in the base, because of the greater ease with which solution in the lachrymal secretion is effected.

**ŒSTRINUM**

(with other OVARIAN SUBSTANCES and MALE HORMONES)

*B P C**Syn* FOLLICULIN.*Dose.*—*See* below.

**Œstrin** is the generic name given to the œstrus-producing substances of the ovaries. The parent substance is the saturated hydrocarbon œstrane, and the following derivatives are known—

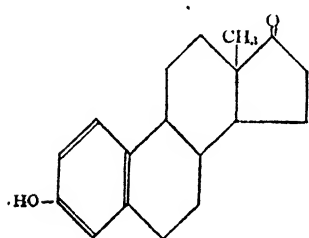
**Œstrone**—a ketohydroxy derivative—3-hydroxy-17-keto-1.3.5-œstratriene,  $C_{18}H_{22}O_2$ , (I). Occurs in colourless dextrorotatory crystals, m p.  $254^{\circ}$  to  $257^{\circ}$ .

**Œstriol**—a trihydroxy derivative—3.16.17-trihydroxy-1.3.5-œstratriene,  $C_{18}H_{24}O_3$ , (II). M.p. about  $279^{\circ}$ .

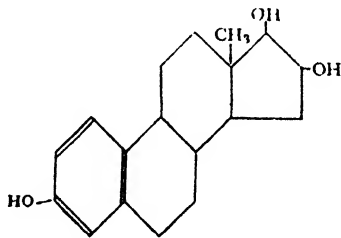
Œstrone, also known as the follicular hormone, and œstriol, also known as the follicular hormone hydrate, may be prepared from pregnancy urine and from ovaries.

**Œstradiol.**

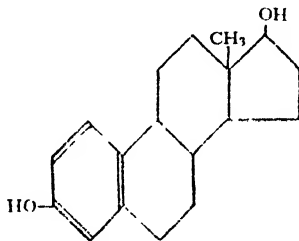
By hydrogenation of œstrone a third derivative of œstrane—a dihydroxy derivative, œstradiol, is obtained. It has the formula (III).



I.



II.



III.

These compounds are characterised by the property of transforming the vaginal epithelium of ovariectomised rats or mice from the diœstrous to the œstrous form. This property serves as the basis of the method of biological assay which is described in Vol. II. The standard preparation is a standard œstrone of which 0.1  $\gamma$  (0.0001 mg) is 1 international unit of activity and this is about one-third of the original Allen-Doisy rat unit. When tested on ovariectomised rats or mice œstradiol is more potent than œstrone.

Substances capable of producing the proliferation of the vaginal epithelium of ovariectomised rats or mice have been found in materials other than reproductive tissues of animals. The term "œstrogenic substances" has been used to include all such substances. The method of expressing the œstrus-producing activity in terms of an animal reaction (*i.e.* as rat units or mouse units) without reference to the standard preparation, is unsatisfactory because it is not possible to make any direct comparison between the rat unit and the mouse unit unless precisely the same technique is followed in each case. Œstrone is sparingly soluble in water, more soluble in oil. Œstrone benzoate is soluble in oil and is used as a means of giving large doses. The activity of œstriol is less than that of œstrone or œstrone benzoate when given hypodermically but greater than either of these when given by mouth. The international unit of dihydroxyœstrin benzoate is 10.555 mg of the standard preparation of dihydroxyœstrin benzoate.

**Separation from Urine.** Crude concentrates of urine are treated with 50% methyl alcohol and light petroleum, the alcoholic layer is separated and treated with ether. The residue, after evaporation of ether, is treated with methyl alcohol (50%) and benzene. Œstrone dissolves in benzene and can be purified by recrystallisation. Œstriol dissolves in the alcohol, it is extracted by ether after acidification, and further purified by extraction with sodium hydroxide.

Tungstic acid method for extraction of œstrin —S. C. Freed, I. A. Mirsky and S. Soskin, *J. biol. Chem.*, 1935, 112, 143.

Methods for the extraction of œstrin and gonadotropic hormone from the same sample of urine —S. C. Freed and O. Hechter, *Endocrinology*, May, 1935, 396.

Rapid method for isolation of œstrone from urine of pregnant mares. High yields claimed by extraction with toluene after evaporation and hydrolysis—œstrone is precipitated as a mercury complex to separate it from non-ketonic phenols and the mercury compound hydrolysed —Beall and Marrian, *J. Soc. chem. Ind., Lond.*, 1934, 309T.

Isolation of œstrin from stallion urine—product identical with that from human pregnancy urine —Deuloffen and Ferrari, *Nature, Lond.*, 1/1934, 935. Also B. Zondek, *ibid.*, 494.

The **production of œstrin** by the ovary is controlled by the gonadotropic hormones secreted by the anterior lobe of the pituitary gland.

Administration of follicular hormone over a long period inhibits the anterior lobe of the pituitary so that the growth hormone and the gonadotropic hormone are not active. Dwarfed animals with hypoplastic genitals result. The dysfunctioning pituitaries of such rats are enlarged and their weight may amount to four times the normal. This increase occurs in male rats only. However, a



very large tumour of the pituitary, produced in a female rat, was 20 times the normal size of the gland—B Zondek, *Lancet*, i/1936, 778

At the end of each menstrual period the immature follicle is acted upon by one of these gonadotropic hormones (prolan A or rho I) which causes it to ripen. At the same time the ovary secretes œstrin which stimulates the uterine musculature until about the fourteenth day when the follicle ruptures, releasing the ovum. Then another hormone from the anterior pituitary (prolan B or rho II) effects luteinisation of the ruptured follicle forming the corpus luteum. The latter secretes the hormone progesterone, which collaborates with œstrin and prepares the mucous membrane for nidation of the ovum. During pregnancy large quantities of the anterior pituitary hormones and of œstrin appear in the urine

**Uses.** The use of these compounds in therapeutics is almost entirely restricted to disorders associated with ovarian deficiency, especially disorders of menstruation and of the climacteric. They have been used in hæmophilia on the theory that, as this condition never occurs in women though it is transmitted through the female, it might be held in check by the follicular hormone. Reports of their value in this condition are contradictory. Gonococcal vaginitis in children has been treated with œstrus-producing hormone

**Dosage**—The doses recommended by different writers range from 500 to 50,000 international units, or more

In 30 patients a total of 100,000 to 200,000 rat units of œstrin produced no appreciable effect on body weight, blood-pressure, basal metabolism, blood count, coagulation time, bleeding time and urine—Mazor, Keranze and Israel, *J Amer med Ass*, ii/1935, 257

Doses of 100,000 to 1,000,000 international units recommended for treatment of amenorrhœa—C Kaufmann, *Proc R Soc Med*, 1934, 849 (*See also* Vol II 20th Edn, p. 146)

The therapeutic use of œstrogenic substances A general review—E Novak *J. Amer. med. Ass*, i/1935, 1815.

Observations on the gynæcological aspects of endocrinology—E Novak *Brit. med J*, ii/1933, 553

Relief of menopausal hypertension and amelioration of all the associated symptoms by administration of œstrin in 13 cases—L Schæfer, *Endocrinology*, 1935, 19, 695.

Clinical experience with œstrogenic preparations has gone beyond the point at which their efficacy can be considered due to suggestion. Oral administration requires five times the dosage for hypodermic injection—E L Sevringhaus, *J Amer med. Ass*, i/1935, 624

Doses of 500 rat units (about 1500 international units) hypodermically on alternate days together with oral administration of œstrogenic substance suggested for relief of menopausal disturbances—*J. Amer. med Ass*, ii/1936, 59.

Two forms of endocrine therapy have been proposed for primary dysmenorrhœa, œstrogenic substance and (in the absence of progestin commercially) urinary gonadotropic substance. As shown in a study of 39 patients, both forms of organotherapy are disappointing. Urinary gonadotropic substance (Antuitrin-S) administered to 10 patients cured 1 and temporarily relieved 3 of dysmenorrhœa (œstrogenic principle, given orally in small doses (Emmenin liquid or Progyonon tablets) to 16 patients, cured 1 and afforded temporary relief to 3 of the patients. Œstrogenic substance, given hypodermically in large doses (Progyonon-B) to 13 patients, produced no permanent results. Ten patients were temporarily relieved and 3 were totally unaffected by the therapy—S L Israel, *J Amer med Ass*, i/1936, 1701

Considerable recovery in 18 out of 22 cases of cystic disease of the breast treated with œstrin in doses of 2000 to 4000 mouse units daily by mouth or 10,000 to 20,000 mouse units weekly intramuscularly —F Dahl-Iversen, *Lancet*, 1/1936, 1294

Chronic mastitis (mastopathia or mazoplasia) treated with œstrin hypodermically, 150 international units daily for five days preceding each menstrual period —Beckwith Whitehouse, *Surg Gynec Obstet*, 1/1934, 278

High doses of œstrin are usually unnecessary, at any rate for the commoner menopausal symptoms—such as the vasomotor disturbances—and consequently œstrin injections are, fortunately, seldom required. It was his practice to begin with doses of about 500 international units daily by mouth. If this does not control the symptoms, the dose is raised to 1000 units and this is usually completely effective. Certain more serious sequelæ of the menopause, such as pruritus, kraurosis and leukoplakia vulvæ require much higher doses—10,000 to 50,000 units once or twice a week as well as 500 units daily by mouth; provided sufficiently high doses are given, the results are little short of miraculous —P M F Bishop, Discussion at R S M on "Medical Aspects of the Menopause"

The successful treatment of hæmophilia by the oral administration of desiccated ovarian substance was reported by C L Birch (*J Amer med Ass*, 11/1931, 24, and 11/1932, 1566). In a discussion on the subject J Brem and J S Leopold (*J. Amer med. Ass*, 1/1934, 200) state that there is considerable doubt concerning the relationship of female sex hormone to hæmophilia, and L L Tureen (*Amer J med Sci*, 1934, 188, 216) found that there was no constant decrease in the coagulation time from oral administration or injection of œstrin.

Treatment of vulvovaginitis (20 cases) with Dimenformon by mouth said to be more rapid than other methods, easy of application and quickly diminishes the discharge, thus reducing infectivity —D Nabarro and A G Signy, *Lancet*, 1/1935, 604

Gonorrhœal vaginitis of children treated with œstrin, successful results reported —R M Lewis, *Imer J Obstet Gynec*, 1933, 26, 593.

Doses of 150 to 300 international units of œstrin hypodermically daily, or alternated with œstriol by mouth. Total dosage required to effect a cure varied from 2550 to 25,350 international units —J Brown, *Amer J Obstet Gynec*, 1933, 593

In several cases use of œstrin to treat vulvovaginitis in children followed by precocious sexual development —Sir W Langdon Brown, *Proc R Soc Med*, 1936, 1089

Doses of œstrin totalling 96 mg followed by Pitocin or Pituitrin had no effect on pregnancy when given at or near term in six cases —A Bourne, *Proc. R Soc Med*, 1934, 864

Not possible to procure abortion in the first few months of pregnancy by means of œstrin, when administered near term œstrin is not a reliable means of inducing labour. The authors consider, however, it is the best means of evacuating the uterus in cases of "missed abortion," or intra-uterine death, method successful in 80% of cases and free from risk. Doses of œstrin totalling from 40,000 to 1,000,000 international units used in from 4 to 16 injections at intervals of from 8 to 12 hours. —A L Robinson, M. M Datnow and T. N A Jeffcoate, *Brit med J*, 1/1935, 749

### Œstrin and Cancer.

Experiments on mice have shown the possibility of producing cancerous tumours by painting the skin with solutions of œstrin. The suggestion that œstrin administration might lead to cancer

formation in the human has been the subject of many papers. The position is reviewed in the *Lancet*, i/1936, 324, where the writer does not believe there is any real evidence to support the view that œstrin is carcinogenic.—See also Kennaway, *Proc. roy. Soc., Ser. B*, 1935, 17, 318; E. C. Dodds, *Amer. J. Obstet. Gynec.*, 1935, 301. The latter points out that the similarity in chemical structure between the carcinogenic hydrocarbons and œstrin is not so close as that between the male and female sex hormones, yet no one would suggest that the injection of œstrin might induce male changes in women.

Mammary cancer is the result of hereditary predisposition plus the uninhibited effect of abnormally large amount of œstrin.—A. Lacassagne, *Amer. J. Cancer*, 1936, 27, 217.

Present knowledge indicates the necessity for caution in the prolonged use of large doses, especially in patients in whom there is reason to suspect susceptibility to cancer—Editorial, *J. Amer. med. Ass.*, i/1936, 1093.

The phenanthrene nucleus is not necessary for carcinogenic activity, several compounds which do not possess this structure were shown to be carcinogenic—Morton, Branch and Clapp, *Amer. J. Cancer*, 1936, 26, 754.

### SOME PROPRIETARY PRODUCTS

**Amniotin** (*Squibb, New York, Martindale, London*) Standardised preparations of œstrin

**Glandubolin** (*Richter, London*) Standardised ovarian (œstrus) hormone

**Gynœstryl** (*Anglo-French Drug Co., London*) Ketohydroxyœstrin in oily solution for injection, and tablets or aqueous-alcoholic solution for oral use

**Ketodestrin** (*Parnes & Byrne, London*) Ketohydroxyœstrin. Ampoules contain 500 i.u. in aqueous solution and 1000 to 500,000 in oily solution

**Menformon** (*Organon Laboratories, London*) Ketohydroxyœstrin. Supplied in tablets of various strengths for oral use, in aqueous solution containing 0.0001 g (1000 Doisy rat units) per ml, in oily solution containing 10,000 units per ml, or in suppositories containing 1000 units

**œstroform** (*British Drug Houses, London*) Ketohydroxyœstrin. For oral use, in tablets containing 1000 units, for injection, in solution containing 1000 or 10,000 units per ml

**œstrosolve** (*Parnes & Byrne, London*) Trihydroxyœstrin 5000 units in a readily absorbed base. For local use in vaginal irritation at the menopause

**Ovarium Panhormon** (*Henning, Berlin, Pharmaceutical Products, London*). A biologically standardised preparation of follicular hormone and ovarian substance containing 100, 1000, and 10,000 mice units equivalent to 500, 5000, and 50,000 i.u. respectively. Supplied in dragées or ampoules

**Progynon** (*Schering, London*) Ovarian follicular hormone biologically standardised. *Dose*.—2 or 3 dragées daily (each of 150 mouse units) and 3 to 6 injections of 1 ml. (100 mouse units) weekly

[P1] **Prokliman** (*Ciba, London*). Tablets contain ovarian hormone 0.02 g, Peristaltin (q.v.) 0.015 g, nitroglycerin 0.0002 g, Kryofin 0.2 g, caffeine sodium salicylate 0.05 g. For all forms of climacteric disturbances. (Kryofin is stated to be methylglycolic-acid-p-phenetidin.)

**Theelin** (*Parke, Davis, London*). Solution of ketohydroxyœstrin containing 200 i.u. per ml. **Theelin in Oil**. 1000, 2000 and 10,000 i.u. per ml. *Dose*.—200 to 10,000 units. Functional amenorrhœa, disturbances of the menopause, etc.

**Theelol Capsules** (*Parke, Davis, London*). Trihydroxyœstrin. Each capsule represents 200 i.u. For oral use.

*Note*.—The names Theelin and Theelol are not registered trade-marks. They are the names used by Doisy to describe the ketohydroxy and trihydroxy hormones first isolated by him, and have been recognised by the Council on Pharmacy and Chemistry of the American Medical Association as non-proprietary names, a condition of the recognition being that they shall not be patented, copyrighted nor trade-marked (*J. Amer. med. Ass.*, ii/1936, 1221). In Gt. Britain the names are not commonly used by manufacturers other than the above.

**Thelestrin** (*Carnrick, Newark, N.J., Brooks & Warburton, London*). Solution of ketohydroxyæstrin for hypodermic injection, each ml contains 25 Doisy rat units.

**Tridestin** (*Paines & Byrne, London*) Trihydroxyæstrin in tablets of 500 to 1000 i.u.

**Uden** (*Bayer Products, London*) Ovarian hormone preparation Dose.—2 ml. or 100 mouse units intramuscularly; 3 tablets (or 300 mouse units) *per os*

## OVARIES

The ovary consists of a framework, or stroma, of fibrous connective tissue with some elastic tissue; embedded in this framework are numerous Graafian follicles in various stages of development. As these follicles attain full development they pass towards the surface. At periodical intervals one or more of these follicles ruptures and discharges the contained fluid—the liquor folliculi—and the ovum or ova. After discharge of its contents the follicle becomes filled with blood and cellular tissue and assumes a yellow colour, it is then known as the corpus luteum.

**Ovarian Substance**—the desiccated whole ovaries of cattle or pigs—freed from fat

**Corpora Lutea**—the yellow bodies separated from the ovaries of cattle and pigs—desiccated and powdered

**Ovarian Residue**—the substance of the ovaries of cattle and pigs remaining after separation of the corpora lutea.

Before the isolation of æstrin and progesterone, the hormones of the ovary and corpus luteum respectively, these desiccated preparations of ovarian tissue were used in the treatment of various diseases of menstruation—dysmenorrhœa, menorrhagia, amenorrhœa—disturbances of the climacteric and in hæmophilia. The desiccated powders have been given orally in tablets or in capsules, and extracts have been given hypodermically. Being unstandardised and of doubtful value, they should be replaced by standardised preparations of the respective hormones.

Powdered ovarian substance is characterised by the presence of more or less distorted cubical to low columnar epithelial cells—the nuclei stain a deep blue and cytoplasm a pink colour with Delafield's hæmatoxylin, by the rounded or irregular masses of primary oocytes surrounded by connective tissue elements, rounded to oval interstitial cells containing granules and fat droplets staining bright red with red acid dyes, numerous fibroblasts with forked ends, numerous lutein cells, often in masses, which appear yellow in preparations mounted in water, an abundance of dense connective tissue consisting mainly of collagen fibres which swell and are stained yellow by a mixture of 1% picric acid and 1% acetic acid.

The microscopical structure of powdered ovarian residue is similar to that of ovarian substance except for the almost complete absence of corpora lutea cells.

Powdered desiccated corpora lutea is characterised by numerous lutein cells isolated or in masses, the individual cells are somewhat polyhedral with spheroidal

central nucleus and numerous lutein granules and fat droplets, the groups of lutein cells are intermingled with fine collagen fibres —Microscopical Characters of Endocrine Glands, W Youngken per *Pharm J*, 1/1936, 44

### PROPRIETARY OVARIAN PRODUCTS

**Agomensin** (*Ciba, London*) Water-soluble ovarian substance *Dose*—1 to 3 tablets three times a day or 1 to 4 ampoules, subcutaneously or intramuscularly, 2 or 3 times a week In functional amenorrhœa

[P1] **Climatone** (*Paines & Byrne, London*). Tablets containing the full hormone complement of ovary whole gland, with theobromine-calcium, calcium lactate, nitroglycerin and menthol valerianate. *Dose*—1 or 2 three times daily before meals for 4 weeks, repeated after an interval of one week Menopausal hypertension, flushing, etc

**Crinex** (*Continental Laboratories, London*) Non-albuminous total ovarian extract containing folliculin and all other ovarian hormones in alcoholic solution Supplied as drops In disorders of puberty and menstruation

**Endovarin** (*Endocrines Ltd, Watford*) Whole ovary with follicular fluid added Supplied in tablets, and in ampoules for injection

**Glanduovin** (*Richter, London*). Extract of whole ovarian gland In ampoules and tablets.

**Gynocalcion M** (*Anglo-French Drug Co, London*) A combination of calcium lactate, with manganese, phosphorus, and ovarian and orchitic extracts, in the form of dragées *Dose*—12 to 16 dragées daily for two periods of 10 days a month separated by an interval of 8 days In menopausal disorders

**Homofort Ovarium** (*Richter, London*) Ovarian gland (whole) 0.1 g, ovarian follicular hormone 10 mouse units *Dose*—3 tablets daily In menstrual disorders and menopausal disturbances

**Lipamin** (*Paines & Byrne, London*) Fractionated extract of ovarian residue after removal of œstrin and corpus luteum Tablets or ampoules for secondary amenorrhœa and associated conditions

[P1 87] **Matronax** (*Knoll, Ludwigshafen, Pharmaceutical Products, London*) Ovarian substance  $\frac{1}{2}$  gr, Thyraden  $\frac{1}{10}$  gr, Bromural  $2\frac{1}{2}$  gr, calcium diuretin 2! gr For menopausal disorders

**Ovacliman** (*Richter, London*) Bromised ovary (80% ovary, 20% bromine) 0.05 g, theobromine 0.05 g, calcium lactate 0.2 g, benzyl succinate 0.03 g *Dose*—1 or 2 tablets thrice daily Menopausal disturbances

[P1 87] **Ovacoids** (*Reed & Carnrick, Jersey City, Coates & Cooper, London*) Fresh ovary 5 gr, fresh anterior pituitary  $\frac{1}{2}$  gr, organic phosphorus  $\frac{1}{10}$  gr *Dose*—2 tablets thrice daily Menopausal disturbances

**Ovamammoid Compound Capsules** (*British Organotherapy Co, London*), contain 1 gr each of ovarian extract and mammary gland extract *Dose*—1 thrice daily  $\frac{1}{2}$  hour before meals and one at bedtime Used in neurasthenia, hysteria, insomnia, chlorosis, amenorrhœa and dysmenorrhœa. Stated to be a galactagogue and emmenagogue

**Ovaraden** (*Knoll, Ludwigshafen, Pharmaceutical Products, London*). Dried ovarian substance—1 tablet equals about 0.5 g of fresh gland *Dose*—Average, 1 tablet thrice daily Dysmenorrhœa and menopausal disturbances

**Ovarnon** (*Organon Laboratories, London*) Tablets containing 0.15 g of desiccated ovarian gland with 10 units of Menformon For ovarian disorders

**Ovobrol** (*Hoffman-La Roche, London*) Ovarian-bromide preparation in the form of soup cubes each corresponding to 1 g of fresh gland (20 mouse units) and 1 Sedobrol cube (=17 gr. of sodium bromide). Ovarian hypofunction

[P1 87] **Panatone** (*Paines & Byrne, London*) Tablets contain ovary (w.g.)  $\frac{1}{2}$  gr., testis  $\frac{1}{2}$  gr., thyroid  $\frac{1}{10}$  gr., pituitary (w.g.)  $\frac{1}{10}$  gr., suprarenal (w.g.)  $\frac{1}{10}$  gr *Dose*—1 to 4 tablets thrice daily. Also supplied as elixir. Menstrual disorders.

[P1 87] **Polyglandin** (*Allen & Hanburys, London*). 5-gr. capsules each containing fresh mixed glands, pituitary  $\frac{1}{2}$  gr., thyroid  $\frac{1}{2}$  gr., ovary  $2\frac{1}{2}$  gr., testes  $2\frac{1}{2}$  gr *Dose*—1 or 2 capsules two or three times daily Neurasthenia, melancholia, infantilism, amenorrhœa, dysmenorrhœa, etc

[P1 87] **Taba. Menocrin** (*Endocrines Ltd, Watford*) Tablets containing whole ovary with follicular fluid, thyroid, total pituitary, magnesium phosphate, calcium

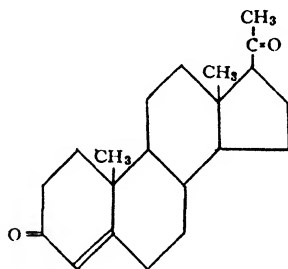
phosphate (dibasic) and glycerophosphate, potassium and sodium bicarbonates. Also supplied in ampoules for injection. Amenorrhœa, dysmenorrhœa, menopause, etc.

[P1-81 87] **Thelygan** (Henning, Berlin, *Pharmaceutical Products, London*). Ampoules containing fresh ovarian extract, ovarian hormones, anterior pituitary, thyroxine, vitamin E, yohimbine hydrochloride, arsenic and strychnine. Tablets are supplied of similar composition but with calcium hypophosphite and yohimbine alkaloid in place of the last three ingredients. *Dose*—1 tablet three times daily or one intramuscular injection (1 ml) every second day.

[P1-87] **Thyrovarian Compound Tablets** (Parke, Davis, London). Desiccated ovarian substance, desiccated suprarenal gland, desiccated thyroid gland. *Dose*—1 tablet twice daily in various manifestations of ovarian insufficiency.

**Varium** (Burroughs Wellcome, London) is a brand of ovarian substance in 5-gr. tablets.

**Progesterone.** *Syn.* PROGESTIN. The hormone of the corpus luteum. A crystalline diketone,  $C_{21}H_{30}O_2$ . Can exist in two forms,  $\alpha$ -progesterone, *m p*  $128^\circ$ , and  $\beta$ -progesterone, *m p*  $121^\circ$ .



Progesterone is standardised biologically according to its effect in causing proliferation of the lining membrane of the uterus in immature rabbits previously sensitised by injections of œstrone.—*See Vol II, 20th Edn., p 146.*

The international unit is the amount of progestational activity present in 1 mg of  $\beta$ -progesterone—adopted by a conference held in London, July 1935, under the auspices of the League of Nations.

The method of assay described by G. W. Corner and W. M. Allen (*Amer J Physiol*, 1929, 88, 326) is conducted on adult rabbits that have been mated and then castrated. A rabbit unit (Corner and Allen) is that amount of the hormone which, divided into five daily doses, produces on the sixth day a state of the uterus equal to that of the eighth day of a normal pregnancy. The Clauberg unit is measured on immature rabbits of 600 g. weight, which are given ten doses of œstrin preceding the five-day course of progestin. This Clauberg unit appears to represent about one-half the potency of the Corner-Allen unit, although it is often stated to represent only one-fifth. In German clinical literature use is sometimes made of a so-called "clinical unit" which is one-third of a Clauberg unit. The international unit is equal to one Corner-Allen unit.—G. W. Corner, *J. Amer med Ass*, 1/1935, 1899.

The corpora lutea of the whale as a source of progesterin. Whale corpora lutea average 2 to 7 kg in weight and the oil obtained from them has an activity of from 20 to 40 units per kg of the wet tissues—Callow, Laurie and Parkes, *J. Soc. chem. Ind., Lond.*, 1935, 1025, see also *Lancet*, 11/1936, 229

**Dose.**—1 to 2 rabbit units by intramuscular injection; it is ineffective orally.

**Use.** Progesterone is used in threatened or habitual abortion and in certain menstrual disorders.

Corpus luteum therapy—functions of progesterone discussed—G W Corner, *J. Amer. med. Ass.*, 1/1935, 1899

Indications for the clinical use of progesterin—P M F Bishop, F Cook and A. C. Hampson, *Lancet*, 1/1935, 139

The female reproductive system—a general review of the hormones of the ovary and corpus luteum—*Prescriber*, 1936, 191

Progynon-B stimulates contraction of puerperal human uterus in doses of 20,000 or 40,000 rat units Progesterin inhibits contractions of human uterus One rabbit unit of progesterin completely nullifies effect of 1 ml of pituitary extract 34 out of 41 cases of threatened and habitual abortion treated successfully with progesterin—Falls, Lackner and Krohn, *J. Amer. med. Ass.*, 1/1936, 271

**Amfetin** (Lilly, London) Amniotic fluid concentrate for stimulating normal processes of repair in operations involving the peritoneal cavity Ampoules contain 50 ml

**Colutamin** (Richter, London) Water-soluble preparation of corpus luteum. **Dose.**—1 ml by injection daily or 2 to 3 tablets thrice daily In amenorrhœa and sexual deficiency

**Colutoid** (Richter, London) Lipoids of corpus luteum **Dose**—1 ml intramuscularly daily, or 1 to 2 tablets thrice daily In menorrhagia, dysmenorrhœa, etc

**Gestone** (Paines & Byrne, London) Progestational hormone of corpus luteum standardised on its rabbit-unit content, one rabbit unit being the amount which produces complete decidual proliferation in four days **Dose**—1 or 2 units intramuscularly daily Habitual and threatened abortion, vomiting of pregnancy, functional menorrhagia, dysmenorrhœa, etc.

**Lipo-Lutin, Improved** (Parke, Davis, London) A solution of progesterin containing 1 rabbit unit per ml **Dose**—1 to 2 ml Habitual abortion, uterine hæmorrhage, etc.

**Luteogan** (Henning, Berlin, Pharmaceutical Products, London) A biologically standardised corpus luteum hormone in an oily solution 1 ml contains 1 rabbit unit or 3 clinical units **Dose**—2 ml injected daily till hæmorrhage ceases Pathological genital hæmorrhage of ovarian origin, habitual abortion, etc

**Luteolipoids** (Paines & Byrne, London) Extract of corpus luteum containing an unspecified amount of the corpus luteum hormone in tablets containing  $\frac{1}{2}$  to  $\frac{1}{4}$  gr **Dose.**— $\frac{1}{2}$  to 1 gr thrice daily during the period of bleeding in menorrhagia and metrorrhagia

**Lutren** (Bayer Products, London) Oily solution of the corpus luteum hormone containing 2 rabbit units per ml.

**Proluton** (Schering, London) Solution of corpus luteum hormone Ampoules contain 2 or 20 clinical units (3 clinical units = 1 rabbit unit). Irregular and excessive uterine hæmorrhage due to ovarian dysfunction; also for habitual abortion.

**Sistomensin** (Schering, London). Liposoluble ovarian hormone isolated originally from the corpus luteum, also obtainable from the placenta. For functional dysmenorrhœa, hæmorrhages of puberty and menopause, menopausal disturbances, etc In tablets of  $\frac{1}{4}$  gr, or 1 ml ampoules containing  $\frac{1}{4}$  gr. in oily solution. **Dose.**—1 to 3 tablets three times a day, or 1 or 2 ampoules a day. Subcutaneously or intramuscularly.

### Placental Hormones

At least three biologically active substances have been obtained from the human placenta. (1) Ether-soluble substances of the

œstrin type, comparable to œstrone or œstriol, and obtained by ether extraction of an acidified aqueous extract, or of alcohol-soluble fractions from the latter. (2) A substance insoluble in ether and alcohol, without effect on ovariectomised animals but capable of causing development of the follicles and luteal tissues in the ovaries of immature rats. This substance is termed the anterior-pituitary-like principle (A.P.L.) and is probably identical with the substance of similar properties in human pregnancy urine (See page 659.) (3) A substance termed **Emmenin** which is not soluble in ether and has little biological activity when tested on ovariectomised animals but causes precocious appearance of œstrus when tested on immature rats, it is more soluble in alcohol and acetone than the anterior-pituitary-like principle. Emmenin gives rise to œstrin on hydrolysis by acids and is probably an ester of œstrin with some unidentified substance.

**Dose**—In dysmenorrhœa, which it has relieved, the equivalent of 25 g of placenta daily for 17 days, beginning with cessation of menstrual period, increasing during week preceding menstruation to 75 g daily, continued till onset of flow and then stopped for a week

The chemical nature of emmenin.—J B Collip, J S L Browne and D Thomson, *Endocrinology*, 1934, 18, 71

Human pregnancy urine contains substances of the emmenin type. According to the work of Marran 99% of the total œstrin excreted during pregnancy is present as an ether-insoluble combined form which shows a low biological activity by the usual tests for œstrin.—S L Cohen, G F Marran and M Watson, *Lancet*, 1/1935, 674

Emmenin in the treatment of dysmenorrhœa—a valuable form of supplemental hormone therapy when the pains have a definite origin from possible uterine contractions. Under treatment with emmenin combined with iron, diet and rest, 49 patients out of 105 had complete relief from pain and associated symptoms, in 27 there was no return of pain after six months without treatment, and 29 were unaffected. The dose recommended is 3 dr daily for a period beginning two weeks before the ensuing menstruation, with a minimum course of ten days' treatment.—M C Watson, *Canad med Ass J*, 1935, 32, 609

Emmenin deserves a place in the therapeutics of menstrual disorders. Helpful in amenorrhœa, if periods have been absent for less than a year, in oligomenorrhœa, hypomenorrhœa and menopausal symptoms, severe dysmenorrhœa appears to be its most useful clinical application. Its chief advantage is its effectiveness by mouth.—M B Goldberg and H Lesser, *Endocrinology*, 1935, 19, 649

**Emmenoplex** (*Glaxo Laboratories, London*) Standardised preparation of emmenin combined with undetermined amounts of œstrin and other ether-soluble principles. **Dose**.—1 to 3 dr daily. Menopausal disturbances, dysmenorrhœa, menstrual headache and oligomenorrhœa

[P1 87] **Ocenta** (*Promonta, Hamburg, Pharmaceutical Products, London*).

Placenta extract, anterior pituitary extract, vitamins, phosphorus, calcium, iron, albuminoids and "readily assimilable carbohydrates," in powder form. **Dose**.—1 or 2 teaspoonfuls 3 or 4 times daily. Lactagogue

#### Placental Extract in Measles.

An extract of human placenta containing the measles antibody termed the "measles immune globulin" has been used for passive immunisation in measles. **Dose**—4 ml. injected into the gluteal muscle, immunity persists for 3 to 4 weeks. Used also in treatment in doses of 2 to 4 ml.—*Pharm. J.*, 1/1936, 653

Doubtful whether the injection of sufficiently large doses to give complete protection is justifiable outside institutions, except in cases of debilitated,



tuberculous or other acutely or chronically affected children. Rather the immune globulin should be used to modify the disease and presumably thereby to render the patient permanently immune. American workers are of the opinion that it is at least as effective as the most potent globulin serum — *Pharm. J.*, 1/1936, 739

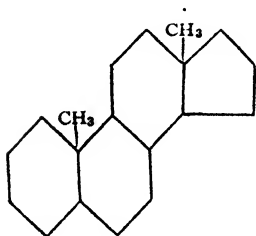
**Embryonin** (*Bioglan Laboratories, Hertford*) A placental extract in 1 ml ampoules. Advocated for the prevention and modification of measles.

## TESTIS

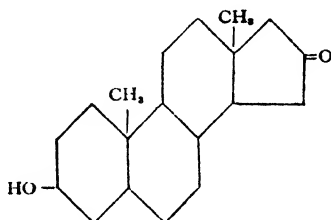
Three distinct chemical substances—"male hormones"—have been obtained from testis tissue or from the urine of males. Other related substances have been obtained synthetically from sterols and bile acids

**Androsterone.**  $C_{19}H_{30}O_2$  M p  $178^\circ$ .

A hormone obtained from the testes of mammals and from the urine of human males. The amount present in male urine is extremely small; Butenandt estimates that about two million litres contain 1 g. It has been prepared synthetically from cholesterol. It has the property of stimulating the growth of the combs of capons and causes growth of the accessory reproductive glands. Androsterone benzoate is inactive. It is a derivative of androstane, *i.e.* androstanolone, 3-cis 17, or 3-cis hydroxy-17-keto androstane.



Androstane  
 $C_{19}H_{32}$



Androsterone  $C_{19}H_{30}O_2$   
3-cis hydroxy-17-keto androstane

Preparation from male urine —A Butenandt, *Z. angew. Chem.*, 1931, 44, 905.  
Synthesis from cholesterol —L Ruzicka and others, *Helv. chim. Acta*, 1934, 17, 1395

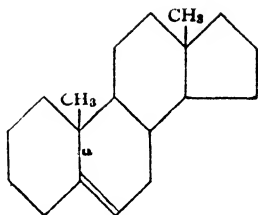
Experiments on rats to determine the effects of the testicular hormone and of oestrone —V Korenchevsky and M. Dennison, *Proc. R. Soc. Med.*, 1935, 1265

Rapid growth of the comb follows injection of 2.5 to 5 mg daily, 1 mg daily will maintain comb at normal level —R K Callow and A S. Parke, *Brit. med. J.*, 1/1936, 527.

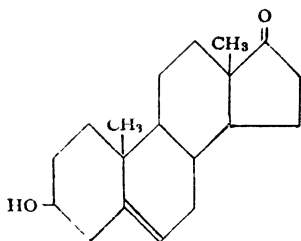
International standard of male hormone is 0.1 mg. of androsterone —P Hartley, *Pharm. J.*, 11/1935, 625

**Dehydro-androsterone** (or dehydroisoandrosterone),  $C_{19}H_{28}O_2$ , is obtained from male urine.

It has physiological properties similar to androsterone but requires about five times larger dose.

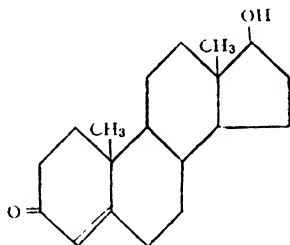


$\Delta^5$ -Androstene.  
 $C_{19}H_{30}$



$\Delta^5$ -Androstenedione-3-trans-17,  
or 3-trans-hydroxy-17-keto- $\Delta^5$ -androstene.

**Testosterone.**  $C_{19}H_{28}O_2$  M.p  $154^\circ$  A crystalline hormone isolated from the testes of rats More active than androsterone



$\Delta^5$ -Androstenedione 17, 3 or 3-keto-17-hydroxy- $\Delta^5$ -androstene

16 to 18 gamma of testosterone is equivalent in comb-growth promoting activity to 100 gamma of androsterone Testosterone is more than twice as active as androsterone on the prostate and ten times as active on the seminal vesicles Methyl testosterone is less active on capons but more active on rats than testosterone Testosterone benzoate is comparatively inactive —R Deansley and A S Parkes, *Brit med J*, 1/1936, 527

The real function of the testis hormone (or hormones) is to control the accessory reproductive organs, it is not a stimulant of male sexual function and has not yet found any very definite clinical applications Its use in treatment of enlarged prostate has been suggested and (*Munch med Wschr*, May, 1935, 787) claims have been made for the successful treatment of a number of cases of enuresis with testicular extract —*Prescriber*, 1936, 204

The physiological activity of the hormone in testis extracts is destroyed by treating with boiling alkali, whereas that obtained from urine is not affected by such treatment —T F Gallagher and F C Koch, *J biol Chem*, 1934, 104, 611

Preparation of testosterone —K David, E. Laqueur and others, *Hoppe-Seyl. Z*, 1935, 233, 281.

Synthesis from cholesterol —L. Ruzicka and A. Wettstein, *Helv. chim Acta*, 1935, 18, 1264.

Nomenclature of "male hormones"—a summary of the compounds having male hormone action, with structural formulæ.—Report of Council on Pharmacy and Chemistry, *J. Amer. med. Ass.*, ii/1936, 210.

The term androgen is suggested to designate substances possessing the property of stimulating the growth of the combs of capons and other effects employed in the assay of the product. Urinary androgens, testicular androgens or androgenic substances from other sources may or may not contain androsterone, dehydroandrosterone or testosterone.—*J. Amer. med. Ass.*, 11/1936, 212.

### Extraction of Male Hormones.

Bull testicles are ground to a pulp and extracted with alcohol (95%) at room temperature. From the alcoholic extract after concentration the active principle is removed by benzene, which is evaporated *in vacuo* and the residue taken up in acetone and allowed to stand at  $-10^{\circ}$  for some hours. Evaporation of the acetone and suspension of the solids in olive oil gives a potent preparation suitable for animal injection. Further reduction of solids is effected by dissolving in alcohol 70% and removing inert material by shaking with hexane. Evaporation of the alcohol yields an oily residue which can be further purified and which is dissolved in ether and shaken with 10% NaOH solution; the majority of the activity remains in the ether.

Urine is acidified with sulphuric acid to approximately 1% by volume, filtered and extracted with benzene. After evaporation of the benzene the residue is taken up in ether and shaken with 10% NaOH; the ether is evaporated to dryness and the residue further purified by fractional distillation under a high vacuum at  $150^{\circ}$  and further purified by use of methyl alcohol, ethyl alcohol and carbon tetrachloride.

The preparation of crystalline material from the crude oil obtained from urine involves hydrolysis and fractionation with organic solvents and treatment of the aqueous-alcohol soluble fraction with hydroxylamine—C. R. Moore, *ref. J. Amer. med. Ass.*, 1/1935, 1406.

### SOME PROPRIETARY PRODUCTS.

**Androstin** (*Ciba, London*) Total testicular extract. Ampoules *A* Hydro-soluble extract from spermatogenic glands, *B* Liposoluble extract from interstitial cells. Injected alternately intramuscularly, in various neuroses and psychoses. Tablets contain total active principles of 8 g. of fresh gland; *dose*—3 to 8 daily.

**Erugon** (*Bayer Products, London*). Standardised testicular hormone. *Dose*.—1 ml. intramuscularly daily or 2 to 3 times a week for 10 injections. Functional disturbances of the male generative glands, neurasthenia, etc.

**Gynofort** (*Richter, London*) Tablets containing testis 0.18 g. and seminal vesicle 0.02 g. *Dose*.—1 to 3 tablets thrice daily. In frigidity.

**Hombreol** (*Organon Laboratories, London*) Male testicular hormone biologically standardised. *Dose*.—1 ml. intramuscularly. In prostatic hypertrophy, etc.

[P1-81-87] **Homovir** (*Anglo-French Drug Co., London*) Tablets containing thyroid 0.005 g., suprarenal 0.018 g., pituitary (whole) 0.03 g., prostate 0.03 g., orchis 0.06 g., yohimbine 0.002 g. Also available in ampoules for injection. In impotence, sterility, etc.

[P1-81-87] **Femlir**, for women, contains active principle of ovaries in place of prostate and orchis. Amenorrhœa, dysmenorrhœa, sexual frigidity, etc.

[P1-81] **Orkitone** (*Anglo-French Drug Co., London*) An elixir containing fresh orchitic gland 21.25 g., nucleic acid 0.326 g., disodium methylarsenate 0.05 g., sodium glycerophosphate 50% 0.5 g., saccharated hydro-alcoholic solution to 100 g. *Dose*.—1 tablespoonful thrice daily. Asthenia, nervous debility, etc.

**Perandren** (*Ciba, London*) The propionic ester of synthetic androsterone, available in 1 ml ampoules containing 5 mg., for subcutaneous or intramuscular injection. Suggested for trial in physical and mental fatigue, convalescence, incipient prostatic affections, delayed puberty and premature senility

[P1 81] **Prostatin** (*Paines & Byrne, London*) Prostate, testis, and cerebrin, of each 15 gr. of fresh gland, yohimbine hydrochloride  $\frac{1}{4}$  gr., in ampoules of 1 ml. Sexual impotence and neurasthenia

[P1 81] **Protestin** (*Richter, London*) Brain, prostate, testis and yohimbine. Tablets and ampoules

[P1] **Sterules of Testicular Extract, Sodium Glycerophosphate and Strychnine Hydrochloride** (*Martindale, London*) contain 10 m, 2 gr and  $\frac{1}{50}$  gr respectively

**Testacoids** (*Reed & Carnrick, Jersey City; Coates & Cooper, London*). Tablets representing fresh testicle 25 gr, fresh prostate 5 gr, organic phosphorus  $\frac{1}{10}$  gr. Dose—3 tablets thrice daily. Male hypofunction

**Testamon** (*Organon Laboratories, London*) Dried total testes in tablets. [P1 81 87] **Testifortan** (*Promonta, Hamburg, Pharmaceutical Products, London*) Contains testis, anterior pituitary, thyroid, suprarenal, epididymis and prostate, with yohimbine, niura puama and glycerophosphates. Dose—2 ml. subcutaneously or intramuscularly daily or every other day, with 2 tablets thrice daily

[P1 81 87] **Testogan** (*Henning, Berlin, Pharmaceutical Products, London*) Ampoules containing testicular extract, male hormone, anterior pituitary, suprarenal cortex, thyroxine, vitamin E, with small quantities of yohimbine hydrochloride, arsenic and strychnine. Tablets are supplied of similar composition but containing calcium hypophosphite and yohimbine alkaloid in place of the last three ingredients. Dose—1 tablet 3 times daily or one intramuscular injection (1 ml) every second day

[P1 87] **Thyorchic Compound Tablets** (*Parke, Davis, London*). Desiccated orchitic substance, desiccated suprarenal gland, and desiccated thyroid gland. Dose—1 tablet before meals. For pluriglandular disturbance in the male

[P1] **Tonicine** (*Reed & Carnrick, Jersey City, Coates & Cooper, London*) Liquid gonadal tonic. Male 1 dr = fresh testicle 25 gr, strychnine sulphate  $\frac{1}{10}$  gr, sodium glycerophosphate 1 gr. Female contains ovarian extract in place of testicle

## OLEA ESSENTIALIA

Notes on essential oils and their preparations not included in the following group are given under the drugs from which they are manufactured (see Index)

**Oleum Bergamottæ** (*B.P.C.*) *Syn* ESSENCE OF BERGAMOT. Distilled from the fresh peel of the fruit of *Citrus Aurantium* subsp. *bergamia*.

**Spiritus Coloniensis** (*B.P.C.*) *Syn* AQUA COLONIENSIS. A form of eau de Cologne for use in hair lotions, etc

**Oleum Cajuputi** (*B.P., P. Helv. V.*)

*Dose*.—1 to 3 minims (0.06 to 0.2 ml.)

Distilled from the fresh leaves and twigs of *Melaleuca Leucadendron* and other species of *Melaleuca* (*Myrtaceæ*) and redistilled in steam. Contains 50 to 60% of cineole,  $C_{10}H_{18}O$ .

**Spiritus Cajuputi** (*B.P.*)

*Dose*.—5 to 30 minims (0.3 to 2 ml.). 1 in 10

**Leucadol.** A redistilled oil of cajuput boiling below  $235^{\circ}$ , fractionated from the high-boiling constituents. A yellow liquid, sp gr 0.922, cineole content 78%. Has been employed in chest affections by injecting into the bronchi. It is miscible with iodised oil in all proportions, with which it has been used for diagnosis. Mix with olive oil up to 5% for oleothorax, or weaker for intratracheal injection

**Oleum Niaouli** (*P. Helv. V*). *Syn and Prop Name.* ESSENTIA EX NIAULI (*F. E. VIII*), GOMENOL (*Laboratoires des Produits de Gomenol, Paris, Coates & Cooper, London*). The oil from *Melaleuca viridiflora*. Contains 50 to 60% v/v of cineole. Is given in rhinitis, laryngitis and other diseases of the respiratory system. It is also used in various forms as a general antiseptic. For injection purposes dilutions in olive oil are used, in strengths varying from 2 to 20%.

5% in olive oil used to replace a pleural effusion, harmless and of value. Liquid paraffin has been used in man—it remains unabsorbed for 14 months. Hard paraffin (m.p.  $39^{\circ}$ ) has been tried in rabbits—F. G. Chandler and S. R. Gloyne, "Tubercle," Sept., 1927

**OLEOTHORAX** Olive oil or liquid paraffin with 0.5 to 5% of Gomenol (olive oil preferable). Not an alternative to pneumothorax. Must never be attempted in a virgin pleural cavity. Disinfectant and compressing action on the lung. Chief indication in pyo-pneumothorax, when acute stage has subsided. 5 or 10 ml maximum initial injection, increased to 30 to 50 ml at next injection, and subsequent doses doubled or trebled according to response. Inject by Jübet blood transfusion syringe or a 30-ml. syringe, using short needle with 1 mm bore. Warm the oil, and when treating effusions aspirate first.—H. M. Davies, *Lancet*, 11/1930, 203.

**Ti-tree Oil.** The oil distilled from the Australian tea tree, *Melaleuca alternifolia*. Contains 50 to 60% of terpenes with up to about 8% of cineole and also terpineol, to which the odour is largely due. Is strongly antiseptic (R.W. coefficient about 11) and has been advocated as a non-irritant germicide for general and surgical use.

**Ti-Trol** (*Australian Essential Oils Ltd, Sydney, Fassett & Johnson, London*) Brand of ti-tree oil available as the oil or as a spirituous soapy solution

The following formulæ yield non-poisonous antiseptics having R.W. coefficients of 3.4. Formula A—Cresantol-3 3 ml, ti-tree oil 3 ml, oil of lemon grass 0.05 ml, isopropyl alcohol 10 ml, triethanolamine 5 ml, ricinoleic acid 5 ml, water to 100 ml. Mix the triethanolamine with the ricinoleic acid and a little water, stirring vigorously, dissolve the Cresantol-3 and the oils in the alcohol, mix the two solutions and dilute to volume. The product has a pH of 8.8.

Formula B—Cresantol-3 3 ml, terebene 2 ml., oil of sassafras 1 ml., industrial methylated spirit 10 ml, potassium hydroxide 10% w/v 10 ml, ricinoleic acid 6 ml, distilled water to 100 ml. Heat the potassium hydroxide solution with the ricinoleic acid, dissolve the Cresantol-3 and the oil of sassafras and terebene in the alcohol, mix the two solutions and dilute to volume. The product has a pH of 11.0.—*Pharm. J.*, 11/1936, 273

**Cresantol-3** (*Monsanto Chemicals Ltd, London*) is a halogenated phenolic compound of undisclosed composition.

**Dettol** (*Reckitt & Sons, Hull*) Described as a halogen derivative of xylenol dissolved in a mixture of aromatic essential oils with a neutral solution of a suitable soap. A non-toxic, non-irritant antiseptic for use in surgery, gynaecology, obstetrics, and for instrument sterilisation, etc. R.W. coefficient 3.

A 1% solution kills hæmolytic streptococci and *B. coli*, even in the presence of pus, and its bactericidal activity is little diminished by admixture with soap. It may be used in concentrated form without toxic effects and is well tolerated by the hands, vulva, and even the intact vaginal mucous membrane.—*Brit med. J.*, 11/1933, 725

**Dettol Obstetric Cream.** A non-greasy ointment for use as an antiseptic in midwifery.

**Dettolin.** A concentrated mouth-wash stated to contain dimethylchlorophenyl hydrate 1.02%, menthol 0.12%, Sapo vegetalis 0.5%, Tinct Roseum Aromatica 64.9%, Elixir Glusidi (B.P.C.) 6.0%, Aqua Dest ad 100 vols.

**Amphyl** (Lysol Ltd, London), **Lysantol** (Allen & Hanburys, London), **Neo-Monsol** (Monsol Ltd, London), **Verpine** (C. G. Fox, London) and **Zant** (Evans, Sons, Lescher and Webb, Liverpool) are non-poisonous, non-irritant antiseptics for use in midwifery, for wounds, and as general disinfectants.

**Oleum Cedri** (B.P.C.) *Syn.* OIL OF RED CEDAR, CEDRI LIGNI OLEUM. Chiefly from *Juniperus virginiana* (Pinaceæ), also from chip shavings and sawdust of pencil cedar (*J. americana* and *J. bermudiana*). It yields a stearoptene, cedrene camphor (cedrol),  $C_{15}H_{26}O$ , and the sesquiterpene cedrene,  $C_{15}H_{24}$ , the odour of which is distinct and stronger than the camphor, and taste finally peppery. Oil largely used in perfumery, also, in a thickened form by concentration *in vacuo* and admixture with other substances, in microscopical work with oil immersion lenses.

The oil from *Cedrus atlantica*, *syn.* LIBANOL, has been given in 8-m. capsules, in doses of up to 6 per diem, in phthisis, bronchitis and skin affections. A 25% ointment in soft paraffin has also been used in skin affections.

**Urocedrol** (Anglo-French Drug Co, London) Essential oil of *Cedrus atlantica*, with hexamine camphorate and salol. *Dose*—6 to 10 capsules daily. Gonorrhœa, cystitis, pyelitis, etc.

**Oleum Citronellæ** (B.P.C.) Obtained from *Cymbopogon Nardus*. Ceylon oil (including oil from Burma and the Straits Settlements) contains not more than 10% of citronellal; Java oil contains from 30 to 40%. Used as a perfume for soap and as an insect repellent.

**Oleum Eucalypti** (B.P., U.S.P. XI, P. Helv. V).

*Dose*—1 to 3 minims (0.06 to 0.2 ml) on sugar, emulsified, or mixed with olive oil. U.S.P. XI average dose 8 minims.

Eucalyptus oil is distilled from the leaves of numerous species of *Eucalyptus*. The oils which contain a large percentage of eucalyptol and little phellandrene are used chiefly for pharmaceutical purposes. The most important species now being distilled for oils of this class are *E. polybractea* and *E. dumosa*. Unmixed oil of *E. globulus* is no longer an article of commerce. As the yield of oil varies greatly with the several species this is a controlling factor. The rectified oils of *E. polybractea* and *E. Australiana* are water white; some oils are tinged slightly yellow when freshly distilled. The oil from *E. citriodora* has an odour resembling that of lemon-grass.

**Soluble** in oils, fats, paraffins, about 3 in 1 of alcohol 90%, in about 3 to 5 vols of alcohol 70% and in all proportions in absolute alcohol.

Poisoning effects from 1 to 6 drachms are recorded. Effects were gastrointestinal irritation and cerebral paresis with vomiting and diarrhœa. Treatment by external stimulation, as on the lines of opium poisoning.

Eucalyptus and castor oil taken in error for plain castor oil. Three doses of camphor given hypodermically. *Recovery*.—L. M. Chesney, *Lancet*, 1/1926, 131.

A pugilist took 3 drachms, as understood by "a drop." Intense drowsiness—complete hypnotic effect.—P. C. Garrett, *Brit med J.*, 1/1925, 1172

Poisoning caused by about  $\frac{1}{2}$  oz Cyanosis. Strychnine  $\frac{1}{16}$  gr. hypodermically and mustard 2 dr. by the mouth after vomiting, stomach lavage.—P. Gibbin, *Brit. med. J.*, 1/1927, 1005. See also *ibid*, 1133, and A. Neale, *Brit med. J.*, 11/1927, 520.

**Uses.** Antiseptic and a popular prophylactic, inhaled or sprayed, for influenza and bronchial catarrh. It is also used for colds as a steam inhalation and given internally on sugar. Useful mixed with an equal quantity of olive oil as a rubefacient for rheumatism.

**CHOLERA EPIDEMICS.** Eucalyptus oil 10 m. twice daily has a definite prophylactic effect.—Brooke

**Nebula Eucalypti (B.P.C.)** Oil of eucalyptus 5% *v/v* in light liquid paraffin.

**Nebula Eucalypti Composita.**

Form A Eucalyptus oil 5 m., cinnamon oil 2 m., menthol 12 gr., liquid paraffin containing 2% thymol iodide to 1 oz

Form B Eucalyptus oil 5 m., methyl salicylate 5 m., menthol 5 gr., liquid paraffin to 1 ounce for a common cold.

**Pigmentum Olei Eucalypti et Acidi Salicylici.**

Eucalyptus oil 8, salicylic acid 1, olive oil to 64

Eczema capitis treated by rubbing into the scalp twice a week

**Unguentum Eucalypti (B.P.C.).** 10% in a paraffin basis

**Unguentum Eucalypti et Acidi Borici.**

Eucalyptus oil 40, boric acid 120, soft paraffin to 500 Lessens secretions of rhinitis.

**Vapor Eucalypti (T.H.)**

Oil of eucalyptus 20 m., light magnesium carbonate 10 gr., water to 1 ounce A teaspoonful in a pint of hot water

[P2] **Vapor Eucalypti Compositus (B.P.C.).** *Syn.* ANTI-CATARRHAL SALTS.

Contains phenol, oil of eucalyptus, camphor, oil of Siberian fir, strong solution of iodine and ammoniated alcohol Pine sawdust saturated with the mixture may be used as "smelling salts"

**Vap. Eucalypt. et Pini (N.I.F.).** Oil of eucalyptus 15 m., oil of Siberian fir 15 m., light magnesium carbonate 15 gr., camphor water to 1 oz

**Eucalyptol (B.P., U.S.P. XI, P. Helv. V, Fr. Cx, F.E. VIII)**  
 $C_{10}H_{18}O = 154.1$  *Syn.* CINEOLE, CAJUPUTOL, MENTHAN-1 : 8-DIOL ANHYDRIDE

**Dose.**—1 to 3 minims (0.06 to 0.2 ml.). *U.S.P. XI* average dose 5 minims.

The principal constituent of oil of eucalyptus, which contains not less than 70%. It is preferred to the crude oil for use in oro-nasal inhalers. It may be obtained from the oil by the action of phosphoric acid (Faulding's process), with which it forms a crystalline compound.

**Nebula Eucalyptolis Composita (B.P.C.).** *Syn.* NEBULA THYMOLIS COMPOSITA.

Eucalyptol 8% *v/v*, with camphor, menthol and thymol in light liquid paraffin.

**Pastilli Eucalyptolis (B.P.C.)** contain  $\frac{1}{2}$  m. (0.03 ml.).

**Pastilli Mentholis et Eucalyptolis (B.P.C.)** contain  $\frac{1}{16}$  gr. of menthol and  $\frac{1}{2}$  m. of eucalyptol

**Eucalyptus (B.P.C.).** *Syn.* EUCALYPTI FOLIUM  
The dried leaves of *E. globulus* (Myrtaceæ). Used in asthma, phthisis and chronic bronchitis.

**Tinctura Eucalypti (B.P.C.)** *Dose*— $\frac{1}{2}$  to 2 drachms (1 to 8 ml) 1 in 5.  
Hæmorrhage from superficial wounds is stated to be capable of arrest by internal use of calcium chloride combined with local application of this tincture.

**Oleum Geranii (B.P.C.)** *Syn.* OIL OF ROSE GERANIUM, OIL OF PELARGONIUM. Obtained from the leaves of *Pelargonium odoratissimum*, *P. capitatum* and *P. Radula*. Used for perfuming dusting powders and other preparations.

**Oleum Graminis Citrati (B.P.C.).** *Syn.* INDIAN OIL OF VERBENA, OIL OF LEMON GRASS, INDIAN MELISSA OIL. Distilled oil from entire herb of *Cymbopogon citratus* and *C. flexuosus*. Carminative, with agreeable odour. Contains citral, citronellal, etc. True oil of verbena is from *Lippia citriodora* and has a more delicate odour.

**Herba Melissæ (Fr Cx, P Dan.)** is from *Melissa officinalis* (Labiatae)

**Alcoolat de Mélisse Composé (Fr Cx)** is prepared from fresh flowering melissa, fresh lemon peel, cinnamon, clove, nutmeg, coriander and angelica root.

20 to 25 drops twice a day is also used as an application in rheumatism, etc. For history, see Edn. XVIII, p. 842

**Oleum Juniperi (B.P.C.)**

*Dose*.— $\frac{1}{2}$  to 3 minims (0.03 to 0.2 ml.). Oil distilled from juniper fruits. Sp. gr. 0.862 to 0.890, increasing with age. Soluble (when freshly distilled) 1 in 4 of alcohol 95%, becoming less soluble with age. A diuretic and genito-urinary stimulant.

**Spiritus Juniperi (B.P.C.)** *Dose*—5 to 20 minims (0.3 to 1.2 ml) 1 in 10

**Spiritus Juniperi Compositus.** *Dose*—2½ drachms. Oil of juniper 8, oil of caraway 1, oil of fennel 1, alcohol (99%) 1400, water to 2000

**Vinum Diureticum (P. Helv. V.).** *Dose*— $\frac{1}{2}$  to 1 ounce (8 to 30 ml.). Juniper 15, squill 10, orange peel 10, absinth 5, angelica root 5, sweet flag 5, dry southern wine 1000

**Juniperus (B.P.C., P Dan.)** *Syn.* JUNIPER BERRY. The ripe fruits of *Juniperus communis* (Pinaceæ) containing about 0.5 to 2% of volatile oil. Used principally in veterinary practice

**Oleum Juniperi Ligni.** A trade name for fictitious juniper oil supposed to be made from the wood, but generally a mixture of juniper berry oil and oil of turpentine.

**Oleum Lavandulæ (B.P.)**

*Dose*.—1 to 3 minims (0.06 to 0.2 ml.)

The oil distilled from the fresh flowering tops of *Lavandula officinalis* (Labiatae). English and French oils are available, the former being considered to have the finer odour. English oil contains (B.P. Add.) 7 to 12% w/w of esters, and French oil not less than 35% w/w, both calculated as linalyl acetate,  $C_{11}H_{20}O_2$ . English oil contains cineole which confers a distinctive odour.

**Spiritus Lavandulæ (B.P.C.)** *Dose*.—5 to 20 minims (0.3 to 1.2 ml) 1 in 10.

**Spiritus Lavandulæ (U.S.P. XI)** *Average dose*—30 minims (2 ml) 1 in 20.

**Spiritus Lavandulæ Compositus (B.P.C.)** *Syn.* AQUA LAVANDULÆ. A form of lavender water for use in lotions, etc.

**Tinctura Lavandulæ Composita (B.P.C.).** *Dose*.— $\frac{1}{2}$  to 1 drachm (2 to 4 ml.).

Oil of lavender 1 in 200, oil of rosemary, cinnamon, nutmeg and red sanders wood in alcohol 90%



**Tinctura Lavandulæ Composita (U.S.P. XI).** *Average dose*—30 minims (2 ml.).

Cinnamon 2, clove 0.5, nutmeg 1, red sanders 1, with oils of lavender and rosemary in diluted alcohol to 100

**Oleum Lavandulæ Spicatæ (B.P.C.).** *Syn.* OIL OF SPIKE LAVENDER. From *L. latifolia* and other species. Has a harsher and more terebinthinate odour than oil of lavender, and is used for similar purposes.

**Oleum Menthæ Piperitæ (B.P.).**

*Dose.*—1 to 3 minims (0.06 to 0.2 ml.).

Distilled from the fresh flowering tops of *Mentha piperita* (Labiata). Contains (B.P. Add.) 4.0 to 9% w/w of esters calculated as menthyl acetate,  $C_{12}H_{22}O_2$  and not less than 46% of free menthol.

**Soluble** 1 in 4 of alcohol 70% and 2 in 1 of alcohol 90%; with some samples of oil the solution becomes turbid on addition of more alcohol 90%.

In coryza the use of this oil instead of menthol is advised. Warm a few drops and inhale. It removes headache from pressure in the frontal sinuses.

It has been confirmed radioscopically that peppermint, and in a lesser degree fennel and chamomile, has a sedative effect on the stomach and a mild stimulating effect on the intestines—*Pharm J*, 11/1926, 680

Oil of peppermint increases bile secretion, oil of thyme does not. A 50% solution of camphor in ethereal oils produces paralysis of the bile ducts for a long time; a 20% solution in oil of peppermint produces paralysis for a short time, followed by polycholitis—*Per J Amer med Ass*, 11/1925, 711

Oil of peppermint, given by mouth to man, decreased the gastric secretion even if there was stimulation of the flow of gastric juice by an alcohol test meal or by histamine. The mode of action of the essential oil is obscure, but patients with peptic ulceration benefit from its administration—J Meyer and co-workers, *Arch. intern Med.*, 1935, 56, 88

**Aqua Menthæ Piperitæ Concentrata (B.P.)** *Dose*—5 to 15 minims (0.3 to 1 ml.).

Contains 2% v/v of oil and is approximately 40 times the strength of the distilled water.

**Aqua Menthæ Piperitæ Destillata (B.P.).** *Dose*— $\frac{1}{2}$  to 1 ounce (15 to 30 ml.). Oil of peppermint 1, water 1500; distil 1000.

**Emulsio Menthæ Piperitæ (B.P.C.).** *Dose*—5 to 20 minims (0.3 to 1.2 ml.) 1 in 10 of oil of peppermint emulsified in water with tincture of quillaia

**Spiritus Menthæ Piperitæ (B.P.)** *Dose*—5 to 30 minims (0.3 to 2 ml.) 1 in 10 of alcohol 90%.

**Spiritus Menthæ Piperitæ (U.S.P. XI)** *Average dose*—15 minims (1 ml.) Oil of peppermint 10% in alcohol in which 1% of washed dried peppermint leaf has been macerated for 6 hours

**Syrupus Menthæ Piperitæ (B.P.C.)** *Dose*— $\frac{1}{2}$  to 2 drachms (2 to 8 ml.) Concentrated peppermint water 1, syrup to 8

**Mentha Piperita (B.P.C., U.S.P. XI)** *Syn.* PEPPERMINT. *Dose*— $\frac{1}{2}$  to 1 drachm (2 to 4 g.). The dried leaves and flowering tops of *Mentha piperita* (Labiata).

**Oleum Menthæ Viridis (B.P.C., U.S.P. XI)**

*Dose.*—1 to 3 minims (0.06 to 0.2 ml.)

Distilled from fresh flowering spearmint, *Mentha viridis*, and *M. crispa*. Contains 42 to 60% of carvone.

Forms a clear solution with an equal volume of 85% alcohol, the solution becoming turbid on further dilution.

**Aqua Menthæ Viridis Concentrata** (B.P.C.). Dose—5 to 15 minims (0.3 to 1 ml.). 2% v/v of oil. Is approximately 40 times the strength of the distilled water.

**Aqua Menthæ Destillata** (B.P.C.). Dose— $\frac{1}{2}$  to 1 ounce (15 to 30 ml.). 1 in 1000.

**Spiritus Menthæ Viridis** (U.S.P. XI). Average dose.—15 minims (1 ml.). Oil of spearmint 10%, in alcohol in which 1% of washed dried spearmint leaf has been macerated for 6 hours.

**Mentha Viridis** (U.S.P. XI). Syn. SPEARMINT, MINT. Dose— $\frac{1}{2}$  to 1 drachm (2 to 4 g). The dried leaves and flowering tops of *M. viridis*.

**Oleum Pulegii** (B.P.C.) Syn. OIL OF PENNYROYAL.

Dose—1 to 3 minims (0.06 to 0.2 ml.), on sugar or in water.

Distilled from fresh pennyroyal herb, *Mentha Pulegium*. A yellow or greenish-yellow oil containing not less than 80% v/v of pulegone. Mildly irritant to the kidneys and bladder and reflexly excites uterine contractions, is used as an emmenagogue. Is reputed to produce abortion. **Oleum Hedeomæ** from *Hedeoma Pulegioides* has similar properties and is similar in composition.

**Antidotes.** Empty stomach by emetic or stomach tube. Give purgative dose of magnesium sulphate. Demulcent drinks freely. Keep patient warm, hot applications to abdomen. Stimulants, e.g., hot black coffee. Morphine,  $\frac{1}{4}$  gr hypodermically, for pain. Saline infusion if necessary.

**Spiritus Pulegii** (B.P.C.) Syn. ESSENCE OF PENNYROYAL. Dose—10 to 20 minims (0.6 to 1.2 ml.). 1 in 10.

**Mentha Pulegium.** Syn. PULEGIUM, PENNYROYAL. Dose— $\frac{1}{2}$  to 1 drachm (2 to 4 g). The dried leaves and flowering tops of *M. Pulegium*.

**Oleum Rosæ** (B.P.C., U.S.P. XI, P. Helv. V). Syn. OTTO OR ATTAR OF ROSE. Distilled from the fresh flowers of *Rosa damascena*, cultivated in Bulgaria (3000 yield 1). A pale yellow, semi-solid crystalline mass.

**Rosettol.** An artificial otto, probably more penetrating than the natural oil. It is entirely free from stearoptene, i.e., is fluid at ordinary temperatures.

**Aqua Rosæ** (B.P.C.) Triple rose water diluted, immediately before use, with twice its volume of distilled water.

**Aqua Rosæ Triplex** (B.P.C.) The undiluted rose water of commerce.

**Aqua Rosæ Concentrata** (B.P.C.) Contains 1% of oil of rose, and is approximately 40 times the strength of rose water.

**Unguentum Aquæ Rosæ** (B.P.C.) Contains oil of rose, rose water, white beeswax, borax and almond oil.

**Unguentum Aquæ Rosæ** (U.S.P. XI). Spermaceti 12.5, white wax 12, almond oil 56, borax 0.5, rose water 5, water 14, otto of rose 0.02. It must be free from rancidity and is required to be stored in pure tin collapsible tubes.

**Unguentum Rosæ Album** (B.P.C.) Syn. CERATUM GALENI. Contains oil of rose, triple rose water, spermaceti, white beeswax and almond oil.

**Oleum Rosmarini** (B.P.).

Dose.—1 to 3 minims (0.06 to 0.2 ml.).

Obtained by distillation from the flowering tops of *Rosmarinus officinalis*. Contains not less than 2% of esters calculated as bornyl acetate,  $C_{12}H_{26}O_2$ , and not less than 9% of free alcohols calculated as borneol,  $C_{10}H_{18}O$ . Is used, mainly in hair lotions, as Spiritus Rosmarini.

**Spiritus Rosmarini** (B.P.C.) Dose—5 to 20 minims (0.3 to 1.2 ml) 1 in 10 Occasionally used in hair lotions as a mild stimulant

**Oleum Rutæ** (B.P.C.)

Dose.—2 to 5 minims (0.12 to 0.3 ml), in hot water or on sugar

A pale yellow oil with unpleasant odour becoming pleasant in great dilution. Contains about 90% of methyl-nonylketone. An emmenagogue and antispasmodic. Has been given as an enema in mucilage of starch for paralytic ileus.

**Ruta** (B.P.C., P. Helv. V.) Syn RUE, HERBYGRASS Dose—10 to 30 grains (0.6 to 2 g.) The dried herb *Ruta graveolens* (Rutaceæ). The infusion has been used as an emmenagogue.

**Confectio Rutæ.** Dose—1 to 2 drachms (4 to 8 g.) Fresh rue, caraway, bay berries, of each 1½, sagapenum ½, black pepper ½, honey 16. Add the first three in powder by degrees to the sagapenum melted in the honey with water q.s. Carminative and antispasmodic. Sometimes used as enema in infantile convulsions.

[P1-81] **Oleum Sabinæ** (B.P.C.)

[P1] and [81] "*Savin, oil of*"

Dose—1 to 4 minims (0.06 to 0.24 ml.) A violent irritant, has emmenagogue and abortifacient properties. May cause hæmaturia and gastro-intestinal irritation.

[P1-81] **Unguentum Sabinæ** (B.P. '85) Melt laid 10 and wax 3 on a water-bath, add bruised fresh savin tops 8, digest 20 minutes and express through calico. Freshly made is used in conjunction with blisters in rheumatoid arthritis.

[P1-81] **Sabina** (B.P.C., P. Helv. V, Fr. Cx.) Syn SAVIN, SABINÆ CACUMINA. Dose—5 to 10 grains (0.3 to 0.6 g.). P. Helv. V and Fr. Cx. have max. single dose 7½ gr.; max. during 24 hours 15 gr. The fresh or dried young shoots of *Juniperus Sabina* (Pinaceæ). Properties are due to the oil.

The tops of *Juniperus sabina*, when taken orally in large doses, sometimes produce abortion, followed by fairly serious poisoning. Two fatal cases of such poisoning are discussed, in both of which death occurred without abortion having taken place. The oil of sabina is fixed in the lungs, liver, uterus and kidneys, especially in the lungs and kidneys.—M. J. Papavassiliou, per *J. Amer. pharm. Ass.*, 1935, A-342.

## OLEA EXPRESSA

**Oleum Arachis** (B.P., P. Helv. V, P. Dan.) Syn OLFUM NUCIS, GROUND-NUT OIL, PEA-NUT OIL.

Dose.—½ to 1 ounce (15 to 30 ml)

The oil expressed from the seeds of *Arachis hypogæa* (syn GOOBER NUT, MANILLA GRAIN, CHINESE ALMOND). Slightly soluble in alcohol 90%, miscible with ether, chloroform and light petroleum. Resembles olive oil in properties and uses.

**Emulsio Olei Arachis** (B.P.C.) Syn MARYLEBONI CREAM (IMPROVED) Dose.—1 to 2 drachms (4 to 8 ml.). A 50% emulsion of arachis oil containing 300 units of vitamin D per drachm.

**Emulsio Olei Arachis cum Glucoso** (Gt. Orm. H.).

Arachis oil 15 m., saccharated lime solution 4 m., acacia 2½ gr., oil of cassia ½ m., oil of clove ½ m., chloroform ½ m., liquid glucose 30 m., decoction of Irish moss to 1 dr.

**Oleum Gossypii Seminis (B P)**

*Dose.*— $\frac{1}{2}$  to 1 ounce (15 to 30 ml)

The purified semi-drying oil expressed from the seeds of *Gossypium herbaceum* and other species of *Gossypium* (Malvaceæ). It is a yellow, almost odourless liquid with a bland nutty taste. At temperatures below 12° solid fat separates, and if this has occurred the oil should be remelted and mixed before use. It is used for the same purposes as olive oil, especially externally.

Wesson oil is a high grade of cottonseed oil, largely used in America as salad oil, said to be superior to olive oil for making mayonnaise.

**Oleum Palmæ (B P C).** A fat obtained from the fleshy portion of the ripe fruits of the palm tree, *Elæis guineensis*, being expressed after allowing the fruits to ferment. It is an orange to dark red fat with a somewhat violet-like odour. Is used in the manufacture of soap.

**Oleum Rapæ (B P C, P Dan)** *Syn* RAPE OIL, COLZA OIL

The refined oil expressed from the seeds of *Brassica campestris* and other species. A pale yellow, slightly viscous oil with unpleasant taste unless highly refined. Used occasionally in liniments in place of olive oil, largely used for burning and as a lubricant. Is used as an edible oil in India.

**Ravison Oil** is from a wild variety of *B. campestris* found near the Black Sea. It resembles rape oil but differs in chemical constants.

**Oleum Sesami (B P, P Hel V)** *Syn* BENNE OIL, GINGELLY OIL, TEEL OIL

*Dose* —  $\frac{1}{2}$  to 1 ounce (15 to 30 ml) Expressed from the seeds of *Sesame indicum* (Pedaliaceæ). A pale yellow oil not solidifying at 0°. Slightly soluble in alcohol 90%, miscible with ether, chloroform and light petroleum.

It does not readily turn rancid, is easily saponified even by cold process, is a semi-drying oil, neither gummy nor sticky, readily absorbed. It is thinner than cottonseed oil.

It may be used instead of olive oil in various parts of the Empire.

**Oleum Sojæ (B P C)** *Syn* SOYA OIL, SOYA BEAN OIL, SOJA BEAN OIL

Obtained by expression from soya seeds, the yield being 10 to 12%. A yellowish or brownish oil, used for soap-making and for burning. It is also used as an edible oil.

**Soja (B P C)** *Syn* SOYA BEANS. The seeds of *Glycine Soja* (Leguminosæ), cultivated in China and Japan for human use and latterly in America and Europe, chiefly for forage. A method of use in the East is to boil until soft and then ferment in a warm cellar—the resulting “cheese” being known as “Natto.”

It contains 38.5% of protein (on dry) and 20% of fat. For this reason, no doubt, the Chinese and other rice-eating people require so little meat. It contains practically no starch—said to be due to presence of a diastase. Has been used as an addition to diabetic dietary. Soy flour is even more serviceable, containing almost  $\frac{1}{2}$  more protein than the bean, this being due to the removal of the fibrous hulls, which contain but little protein. For further data see Edn. XVIII, p. 860.

and XIX, p. 887. The seeds also contain the enzyme urease, which converts urea into ammonium carbonate. It can be extracted by dilute alcohol or acetone and used in the determination of urea in blood or urine.

**Soya Bean Milk.** The shells are removed after baking the beans overnight in 3 times their weight of water, then ground and boiled for 5 minutes and filtered through a sieve. To every 1000 g of filtrate add 20 g of starch previously made into a paste with some of the filtrate, 60 g of sugar, 15 g of calcium lactate, and 1 g. of salt. The addition of cod-liver oil is essential—*Brit med J. Epit*, 1/1931, 93.

Beans of the mammoth yellow variety are cleansed, treated to remove unpleasant flavour and converted into a milky liquid. Malt syrup, lactose, cotton seed oil, mineral salts (Nemssalz), and calcium lactate are added and the mixture homogenised and spray-dried, being re-liquefied in the proportion of 35 gr to 8 oz of boiled water, providing a greyish-white "milk", in fine suspension, with about the same body as cows' milk. One ounce contains 28 Steenbock units of vitamin D. The "milk" was well tolerated and babies fed on it showed gain of weight and resistance to infection equal to that of milk-fed babies.—F. R. Ruttinger and L. H. Dembo, per *Brit med J*, 1/1933, 378.

**Soyolk** (*Soya Flour Manufacturing Co., Rickmansworth*) A flour made from the soya containing 20% of fat, which does not turn rancid. It has 45% of protein, 16% of carbohydrates, principally sucrose and dextrin, no starch, and vitamins A, B, D, and E. Suggested as a basic food for infants, *etc.*, to blend with other ingredients and reduce the protein and increase the sugar, *etc.*, with lactose.

**Sobee.** A mixture of soya bean flour 67.5% and barley flour 9.5%, with olive oil 19%, sodium chloride 1.3%, and calcium 2.7%. Used as a milk substitute for infants with milk idiosyncrasy. Infants take it well, digest it, and thrive on it—L. W. Hill and H. C. Stuart, *J. Amer. med. Ass.*, 11/1929, 986. See also *ibid.*, 989.

## OLEUM HYDNOCARPI

B.P.

**Dose.**—5 to 15 minims (0.3 to 1 ml.) gradually increased to 1 drachm (4 ml.); by subcutaneous or intramuscular injection,  $\frac{1}{2}$  drachm (2 ml.) gradually increased to 75 minims (5 ml.).

Obtained by cold expression from the seeds of *Hydnocarpus Wightiana*, and occurs as a yellowish or brownish-yellow oil or soft cream-coloured fat. Contains glycerides of hydnocarpic and chaulmoogric acids.

Oleum Hydnocarpi (*P. Helv. V*) is from *Hydnocarpus Kurzii* (see Oleum Chaulmoogræ).

**Soluble** almost completely in hot 90% alcohol, partly insoluble in cold; miscible in ether, chloroform and carbon disulphide.

**Uses.** Is given *per os*, or by subcutaneous or intramuscular injection in the treatment of leprosy. It is well tolerated if injections are made into healthy subcutaneous tissues, and rarely causes any reactions.

The oil is not suitable for intradermal infiltration over large area. Ester preferable—E. Muir, *Lancet*, 1/1931, 1401.

Hydnocarpus oil with 4% of creosote the cheapest and most effective remedy, and the one which did the maximum amount of good in all stages.—R. G. Cochrane, R.S.M. Discussion, *Brit med J*, 1/1927, 285.

There is no specific cure, but the following clears up active signs in early cases: (1) treatment of accompanying disease, (2) rectification of diet, (3) gradually increasing exercises, (4) injection of hydnocarpus oil and its preparations, (5) external applications, (6) surgical intervention when necessary.

Vaccines intravenously are useful in certain cases and in the third stage of the disease: hydnocarpus oil is the most efficient treatment in the first and second stages—E Muir, R S M. Discussion, *Brit med J*, 1/1927, 284, *Lancet*, 1/1927, 339.

### Sodii Hydnocarpas.

A preparation obtained from the low-melting fraction of the acids of *H Wightiana* oil Has been used in leprosy as the 1 to 3% solution in doses of up to 10 ml.

Sodium hydnocarpate is specially convenient, but apt to cause endophlebitis and block the veins when given intravenously The last Indian Census, 1921, gave the number of lepers as 102,513, but it is believed there are four or five times that number infected Removal of predisposing causes, which lower resistance of patient, are important Erythrocyte sedimentation test is useful in determining degree of resistance Desirability of further botanical research into possibility of introducing hydnocarpus trees in British Possessions in Africa where leprosy is rife—the fresher the seeds the more active the therapeutic action of the oils—E Muir, per *Brit med J*, 11/1930, 1095

Pain of subcutaneous injections markedly reduced by addition of glycerin—2.5 ml of pure glycerin to 100 ml of 3% sodium hydnocarpate solution containing 0.5% of phenol—J T Jackson, per *Brit med J Epit*, 11/1932, 98

A preparation worthy of more than passing attention is sodium hydnocarpate (Alepol) which, in many countries, is used as the drug for routine treatment—E Muir, *Int J Leprosy*, 1933, 441

**Alepol** (*Burroughs Wellcome, London*) The sodium salts of a selected fraction of the lower m p fatty acids of hydnocarpus oil

**Dose**—1 ml of a 3% solution (increased to 5 ml or more) intramuscularly or subcutaneously, intravenously 1 ml of 1% solution increased by 1 ml, up to 5 or 10 ml

Intravenous injections up to 10 ml of 5% solution the method of choice in "mass" treatment in the Yambio District of the Belgian Congo Locally, trichloroacetic acid is used and ulcers dressed with hydnocarpus oil—A Cruickshank, *Leprosy Rev*, Jan, 1932, 6

Ionisation of the nasal mucous membrane, using Alepol, potassium iodide, and sodium chloride, in 1% solution, produces in many cases apparently complete cure of leprotic lesions in this site, an electrode being placed in each nostril and kept in position by bandages, and a current of 20 to 30 ma. passed for 20 to 30 minutes—F G Rose, *Brit med J*, 1/1929, 148

[P2 S1] **Avenyl** (*Burroughs Wellcome, London*) 2-Myristoxy-mercuri-3-hydroxybenzaldehyde, a mercuric preparation for the treatment of leprosy complicated by syphilis Is soluble in hydnocarpus oil and in the ethyl esters of hydnocarpus oil, and may be administered as a 0.25% solution in hydnocarpus oil, or as a 0.5% solution in the ethyl esters in doses of 1 ml, increased to 4 ml or more, in courses of 12 to 15 injections

**Sodium Hydnocarpate Sterules** (*Martindale, London*) contain 10 ml. of 1% solution

**Oleum Hydnocarpi Æthylicum (B P).** *Syn* ETHYL ESTERS OF HYDNOCARPUS OIL, ETHYL HYDNOCARPATE, HYDNESTRYLE

**Dose.**—5 to 15 minims (0.3 to 1 ml), increasing gradually to 1 drachm (4 ml). By subcutaneous or intramuscular injection,  $\frac{1}{2}$  drachm (2 ml.) gradually increased to 75 minims (5 ml)

A colourless or faintly yellow oil with acrid taste Prepared by saponifying the oil and precipitating the acids, dissolving them in ethyl alcohol and esterifying by passing in hydrogen chloride.

Is used for the same purpose as hydnocarpus oil, either alone or mixed with an equal volume of olive oil with or without creosote 4%.

Creosote 4% in equal parts of olive oil and the ethyl esters of hydnocarpus oil, given by subcutaneous infiltration twice weekly, initial dose  $\frac{1}{4}$  ml., increasing

by  $\frac{1}{2}$  ml., has been successful in India.—R. G. Cochrane, *Lancet*, ii/1926, 95

Found useful at Dichpalli, Hyderabad. Of 180 patients treated in 1923-24 17% were symptom-free, 45% improved and likely to be symptom-free, 35% improved and 3% worse or dead. Of infective cases 63% have become non-infective.—Isabel Kerr, *Lancet*, ii/1925, 373. See also *Proc. R. Soc. Med.*, 1927, 135

The toxic action of chaulmoogra oil appears to be due to esters of hydnocarpic acid. Ethyl hydnocarpate intravenously into rabbits causes lower calcium content of blood, with associated hyposensitivity, followed by inco-ordination, death following respiratory failure. The toxic dose is 0.5 ml. per kilo for rabbits.—B. F. Read, *J. Pharmacol.*, 1924, 221.

Intradermal injections of chaulmoogra and hydnocarpus esters should be accompanied by intramuscular to produce maximum effect. Big doses should be pushed where resistance is high—but doses above 10 ml harmful.—R. Cochrane, *Trans. R. Soc. trop. Med. Hyg.*, 1931, 98

The action of hydnocarpus oil and its preparations injected intradermally, is largely due to the local irritation, which continues for some time, the esters remaining absorbed inside the local cells, causing breaking down and phagocytosis of the lepromatous material. There might also be some antigenic action.—E. Muir, *Trans. R. Soc. trop. Med. Hyg.*, 1931, 92

Ethyl esters of the oil of *H. anthelmintica* in prophylactic treatment of leprosy is used in the colonies of the Federation of Indo-China. First week, 1 ml is injected, second week, 1.5 ml, third week, 2 ml, until a dose of 5 ml is reached. Results sufficiently favourable for lepers to ask for injections instead of rebelling against treatment as formerly.—Per J. Amer. med. Ass., ii/1925, 206.

**Eulykol** (*Burroughs Wellcome, London*). Phenyl-ethyl esters of a selected fraction of the acids of hydnocarpus oil, or "phenylethyl hydnocarpate." Dose.—Commence with 0.5 ml intradermally and a week later infiltrate the whole patch with 1 ml., increasing to 2 to 5 ml at weekly intervals until the nodules have disappeared, in other cases the commencing dose may be 2 ml., gradually reduced. *Lupus vulgaris*.

Phenylethyl hydnocarpate of value by intradermal injection in the treatment of *lupus vulgaris*. Of 11 cases treated, clinical cure of affected patches was obtained in 7 and the other 4 showed satisfactory progress. The injections cause comparatively little pain and after treatment very little scarring is present.—N. Burgess, *Brit. med. J.*, ii/1935, 835

**Hydnocarpus Nut.** The powdered nut is the main treatment in an asylum in the Malay Peninsula. A popular Chinese remedy, palatable and inexpensive.—E. A. O. Travers, R. S. M. Discussion, *Brit. med. J.*, i/1927, 285

**Oleum Chaulmoogræ** (*B.P.C.*, *U.S.P. XI*, *P. Argent. II*, *P. Ned. V*, *P. Helv. V*, *P. Belg. IV*, *F.E. VIII*). Incorrectly given the synonym *Oleum Gynocardia* in *B.P.* '14

**Dose.**—5 to 15 minims (0.3 to 1 ml.), increased to 1 drachm (4 ml.) orally, in capsules, cod-liver oil, or milk; 30 minims (2 ml.), increased gradually to 75 minims (5 ml.) by subcutaneous or intramuscular injection. *F.E.* max single dose 1 g., max in 24 hours 5 g. *U.S.P. XI* average dose 15 minims.

The oil (about 33%) expressed from the seeds of *Hydnocarpus Kurzii* (formerly *Taraktogenos Kurzii*). This is an evergreen shrub growing in Chittagong, Burma, and other parts. *U.S.P. XI* includes the oils of *Taraktogenos Kurzii*, *Hydnocarpus Wightiana*, *H. anthelmintica* and other species of *Hydnocarpus*, provided the oil agrees with specification. *P. Helv. V* calls this oil "*Oleum Hydnocarpi*," with *syn. OLEUM CHAULMOGRÆ*.

The kalaw tree, frequently stated to be the historic origin of chaulmoogra oil, is apparently the Burmese name for *Taraktogenos Kurzii*.

*Gynocardia* oil is from *G. odorata*. It has a brown colour and odour resembling painter's varnish, and remains liquid down to

4.5". It does not contain chaulmoogric acid but consists chiefly of the glyceryl esters of linolic and linolinic acids. It is stated to have no therapeutic value in leprosy. The fruits yielding genuine chaulmoogra oil are distinguished from those of gynocardia by containing many seeds (average 21) packed closely together and faceted by mutual pressure, hence no two are the same identical shape, and having no pulp, the embryo is vertical and cordate, while that of gynocardia is lateral and reniform.

The name chaulmoogra has been sometimes misapplied to a smaller seed derived from *Hydnocarpus anthelmintica*, a native of Siam, where it is known as Lukrabao. This is exported to China and used there for leprosy in place of the true chaulmoogra, which may be regarded as the East Indian remedy.

The oil from *Hydnocarpus Kurzii* is cold-drawn. It is a yellow fat, or at tropical temperatures a brownish-yellow oil with an odour of rancid butter and m.p. of 22° to 23°. It consists chiefly of the glycerides of chaulmoogric acid  $C_{18}H_{32}O_2$ , and hydnocarpic acid,  $C_{18}H_{34}O_2$ . The residual cake is valuable for cattle feeding.

**Soluble** in ether and in chloroform.

**Uses.** The oil is applied externally, and given internally *after meals*, for leprosy, phthisis, scrofula, rheumatism, marasmus, psoriasis and lupus. The treatment of leprosy with it has to be persisted in for several years. The theory of its action in leprosy seems to be that it increases the number of leucocytes and enhances the bactericidal properties of the blood. Leprosy has also been treated by ½-ounce doses per rectum daily.

For phthisis 2 to 4 ounces should be rubbed into the chest weekly. Applied to raw surfaces, however, it causes great pain.

INTRADERMAL INFILTRATION undoubtedly gives better results than intramuscular and subcutaneous injections in leprosy. In patients in whom the skin areas involved are too small to permit giving the desired doses by the intradermal route, supplementary intramuscular or subcutaneous injections may be given. The relative efficacy of the oil and esters given intradermally has not yet been fully tested, but experience shows that both are effective, and that if either is better than the other the difference is not great.

**TECHNIQUE.** A small syringe is used with a short guarded needle. If oil is used the temperature must be at least 55°. The area to be injected is marked off with grease pencil and sterilised. Infiltration is made through multiple punctures 6 to 10 mm apart, 0.5 to 1 mm being injected at each puncture, so that to give the maximum 5 ml. dose some 80 to 100 punctures are required. The needle should be sloped at an acute angle with the skin surface and should not enter more than 2 or 3 mm, except for deeper lesions. In patients with marked fibrous nodules, begin treatment by infiltrating them (2 to 4 drops slowly injected into the middle of the nodule), treating the more diffuse lesions later. The dose varies according to tolerance, from 0.5 to 5 ml. once or twice a week. Almost all skin areas showing either visible lesions or deep analgesia due to local invasion by *M. lepræ* are suitable for infiltration (this does not apply to analgesia of the extremities due to affection of the nerve trunks supplying them). When the lesions are widespread it is well to begin with the back of the trunk, as it is less sensitive. As a rule lesions should not be infiltrated a second time within a month. The induration caused by the previous infiltration must first be absorbed, lest much pain and even ulceration occur. Spots of hyperpigmentation remain at old sites of puncture and the new punctures should be made between them. Recommendation of the infiltration method does not exclude other supplementary methods of special treatment, e.g., hot baths, cauterisation,



etc. In a patient who can tolerate maximum treatment and maintain a sedimentation index below 10, a good prognosis can generally be given.—E. Muir, *Int. J. Leprosy*, 1933, 442.

Treatment of leprosy—a valuable review with extensive bibliography—E. Muir, *Int. J. Leprosy*, 1933, 407.

**TUBERCULOUS LARYNGITIS.** Local applications of chaulmoogra oil (Burmese), either diluted 10 to 20% in mineral oil, or full strength, dropped into the larynx or applied by a swab, in ulcerative tuberculous laryngitis, and superficial infiltrations, have been praised by R. M. Lukens, of Philadelphia. R. Scott Stevenson found it soothing but not of any curative benefit—*Brit. med. J.*, 11/1933, 964.

### **Emulsio Olei Chaulmoogræ.**

*Dose.*— $\frac{1}{2}$  to 1 drachm (2 to 4 ml.)

Chaulmoogra oil 1 oz., poppy seed oil 2 oz., powdered acacia  $\frac{1}{2}$  oz., cinnamon oil 6 m., saccharin elixir 45 m., with water to make 6 oz.

### **Injectio Olei Chaulmoogræ Intramuscularis.**

*Dose.*— $\frac{1}{2}$  to 1 ml., increased to tolerance.

Chaulmoogra oil and almond oil equal parts, sterilised.

This and other formulæ have been given intramuscularly, but the injection of oily preparations of chaulmoogra is often badly tolerated—causing abscess, heart failure, etc.

The following is said to be *painless*. Chaulmoogra oil 90, olive oil 10, benzocaine 3. 5 ml. injected at body temperature in deltoid region, alternating semi-weekly with 8 ml. in buttocks.

### **Unguentum Chaulmoogræ (B.P.C.).**

10% in a paraffin basis

### **Sodii Chaulmoogras (B.P.C.)** *Syn* SODIUM GYNOCARDIOL

*Dose.*—1 to 3 grains (0.06 to 0.2 g.).

A mixture of the sodium salts of the fatty acids, or of a selected fraction of the fatty acids, of chaulmoogra oil. Occurs as a granular yellow or buff-coloured powder.

Good results in long-standing infection from the use of sodium chaulmoograte in sufficient quantity to saturate the system to the limit of toleration, treatment extending over months. Intravenously 0.04 g. given every second day, followed by an interval of 25 days after each 12 injections. In some cases a 1% or 1.5% solution was better tolerated than the 3% solution. Found to be one of the best anti-leprosy remedies, intense and rapid in action—E. Balbi, *Brit. med. J. Epit.*, 1/1927.

Sodium chaulmoograte, used with caution, has proved to be tolerated, either intravenously or intramuscularly, over a long period of time, and, in association with local treatment, good food, fresh air, etc., is an anti-leprosy preparation in no way inferior to Antileprol or Collobiase, and, moreover, when used intravenously, has an undoubted beneficial action which is more rapid and intense than that of chaulmoogra oil, though perhaps not so lasting. **Collobiase.**—An emulsion of the formula: Chaulmoogra oil 0.36 ml., acacia 5 g., distilled water 500 ml. *Hypodermically* commence with 1 ml., increased by 0.1 ml. on alternate days, up to a total of 5 ml., which dose is maintained up to the 20th injection. *Intravenously* commence with 0.25 ml., increased by 0.1 ml. on alternate days up to 2 ml., which dose is maintained up to the 20th injection.—Antonio Marras, "La Terapia della Lepra ed i Risultati Ottenuti coi Moderni Trattamenti," University of Cagliari, 1929, p. 133.

**Sodium Chaulmoograte "C" Sterules** (Martindale, London) contain a solution of 1, 2 or 3 grains of the sodium salts of a fraction of the fatty acids of chaulmoogra oil having a m.p. of 25° approx. *Dose.*—An injection may be given deeply under the fat layers—this is stated to reduce reaction—once or twice a week or as found to be tolerated.

**Æthylis Chaulmoogras (U S P. XI)**

*Average dose.*—By mouth or by intramuscular injection, 15 minims (1 ml.).

A pale yellow oil prepared from chaulmoogra or hydnocarpus oil, or from the oil of *H. Anthelmuntica* by the same method as Oleum Hydnocarpæ Æthylicum, which it closely resembles.

The preparation remains in the cells for months, hence mild irritative effect. A desirable psychological effect —E Muir, *Lancet*, 1/1931, 1401. Sir L. Rogers found the effect too irritating.

The efficacy of chaulmoogra in leprosy lies, apparently, not in the use of the ethyl ester, but in that of the whole oil, preferably in conjunction with pyrogallol oxide —T C Ghosh, *Lancet*, 1/1923, 630.

Leprosy in Hawaiian Islands. Most prevalent during school age and most common in male sex. Ethyl esters of chaulmoogra oil of benefit in most cases —W T Corlett, per *J. trop. Med (Hyg)*, 1923, 13.

24 out of 300 lepers cured, and 30 convalescent with ethyl esters —K Shiga, *Indian med Gaz*, 1926, 355.

**Iodised Ethyl Chaulmoograte containing 2% Iodine.**

*Dose* —1 ml intramuscularly has been reported on —See H W Wade and C B Lara, *Lancet*, 1/1927, 599.

**Antileprol** (Bayer Products, London) Ethyl esters of the fatty acid of chaulmoogra oil.

**Moogrol** (Burroughs Wellcome, London) A mixture of esters of the acids of the chaulmoogric series for intramuscular injection in the treatment of leprosy, and also, in combination with 1% of creosote, in lupus vulgaris. **Iodised Moogrol** is Moogrol with 0.5% of iodine, which markedly reduces the irritation produced. Injections are made intradermally and intramuscularly at weekly intervals. Intradermally, 5 ml is given each time, 0.1 ml at each point. If total 5 ml, cannot be given in this way, the balance is given intramuscularly.

**OLEUM MORRHUÆ**

(with CALCIFEROL and VITAMIN A PREPARATIONS)

*B P Add., U S P XI*

*Syn.* OLEUM JECORIS ASELLI (*P G VI, P Ital. V, P. Belg. IV, F E. VIII, Fr. Ca., P Dan*), OLEUM JECORIS (*P Helv V*).

*Dose.*—Prophylactic, 15 to 30 minims (1 to 2 ml) 3 times daily; therapeutic, 45 to 90 minims (3 to 6 ml) 3 times daily. *U S P. XI* average dose 2 drachms.

The oil expressed from the fresh liver of the cod, *Gadus morrhua*, and freed from solid fat by filtration at 0°. *B P. Add.* requires the oil to contain per g not less than 600 units of vitamin A activity, and not less than 85 units of antirachitic activity. These limits are much lower than the proportions of the two vitamins usually occurring in commercial samples of the oil (see Vol. II, 20th Edn, p 164). Inferior brands are prepared by heating.

*U S P XI* states "and other species of the family *Gadidae*." The oil may be flavoured with 1% of recognised flavouring agent. It contains at least 600 i.u. of vitamin A per g, and at least 85 i.u. of vitamin D.

**Oleum Morrhue Non-Destearinatum** (*U.S.P. XI*) is the entire oil, i.e., not destearinated.

Preparations containing antirachitic vitamins of cod-liver oil in a concentrated form are made by separating the unsaponifiable fraction of the oil.

The oil is extracted with formic or acetic acid, and the acid extract, amounting to about 5%, is saponified with alcoholic alkali. The soaps are extracted with ether. This extract gives on evaporation a brown residue (about 0.1% of the oil). Air being excluded, the product is stable for seven or eight months. A 1 g tablet may be made representing the therapeutic activity of a tablespoonful of the oil.—*Pharm J.*, ii/1925, 394

**Soluble** slightly in alcohol 90%, miscible with ether, chloroform, and light petroleum

**Uses.** Nutritive tonic given in rickets, phthisis, chronic bronchitis, general debility and malnutrition. When a patient is for any reason on a “+ lime” diet cod-liver oil should be given.

The oil is absorbed when applied externally by inunction, and can be given to infants in this way. It is also applied in the treatment of wounds and burns, either alone or mixed with soft paraffin. The oil has a bactericidal action and stimulates epithelial growth, the latter effect possibly being due to the vitamin D content.

Capsules of cod-liver oil 19 minims and creosote 1 minim are for use in phthisis, also made plain, 20 and 30 minims.

Taking the oil increases blood calcium—decreases the coagulation time. Pulmonary hæmorrhage with increased coagulation should benefit. As calcium salts *per os* cause rise of blood calcium, intravenous injections are not needed.—*J. Amer. med. Ass.*, ii/1925, 66

**BURNS, VARICOSE ULCERS AND BED SORES** 120 cases treated. A noticeable feature was the absence of pain when dressings were changed.—K. Strauss, *Dtsch. med. Wschr.*, 1935, 50

Very popular with the patients, who experience great relief on its first application. A dressing of lint well soaked in crude cod-liver oil preferred to ointment. The dressing is resoaked with the oil after 24 hours, the lint not being renewed until after 48 hours.—J. P. Steel, *Lancet*, ii/1935, 290

**BURNS OF THE EYELIDS** The first dressing is a pad of lint saturated with the oil, covered with jaconet or oiled silk and a bandage, the patient being instructed to get a bottle of the oil and to keep the pad moist with it, leaving the pad undisturbed for 24 hours. There is never any septic discharge. The pad is changed every 24 hours. For use as drops at home, the easiest way is to pour the oil from a warmed teaspoon rather than use a dropper, which is difficult to keep clean, every 3 or 4 hours. One remarkable point is the almost instant relief from pain.—E. Stevenson, *Lancet*, ii/1935, 1376

**GASTRIC ULCER** Good results were obtained from the administration of cod-liver oil (20 g. 4 times daily) to patients with gastric ulcer when operative treatment was contraindicated. The best response was obtained when the ulcer was situated high in the lesser curvature and the ulcerative process had spread through to the neighbouring organs. Cod-liver oil leads to increase in weight, limits gastric motility and has a local therapeutic effect on the ulcerated tissue.—W. Löhr, per *Nutr. Abstr. Rev.*, Jan., 1936, 795

**INTESTINAL TUBERCULOSIS.**  $\frac{1}{2}$  oz. of cod-liver oil floated on 3 oz. of strained tomato juice, or the juice of an orange, thrice daily after meals, better than ultraviolet radiation. Improvement begins in a few days.—C. F. Møller, *Indian med. Gaz.*, Dec., 1930

**WOUND TREATMENT** Three years' experience of the application of fresh unheated cod-liver oil, mixed with an indifferent oily medium to the consistency of a paste, to suitable wounds, e.g., recent uninfected accidental wounds, burns, compound fractures, amputation wounds, bed-sores, frostbite, etc. Dressing changed as frequently as possible, and contact of the wound with the inner portion of the dressing left undisturbed. Efficacy ascribed to direct vitamin action on the tissues.—W. Löhr, per *Brit. med. J. Epit.*, ii/1934, 86

Treatment of 300 casualty cases from an explosion at a toluol factory, including badly infected compound fracture, open wounds of the joints, extensive muscle

and tendon lacerations, complete removal of the scalp, and severe burns. The immediate surroundings of a wound having been shaved clean, it was filled with a cod-liver oil ointment and then lightly secured with sutures made from the muscles of horses and cattle. Over this was a layer of cod-liver oil ointment, kept in place by an adhesive dressing. Necrotic tissues quickly came away and the depths of the wound became filled with granulation tissue. The ease with which new skin grew rendered transplantation superfluous, although there had been no preliminary sterilisation.—P. Bosse, *Dtsch med Wschr*, 1935, 1638.

### **Oleum Morrhuæ Aromaticum.**

*Dose*.—1 to 4 drachms.

Coumarin 0.01, saccharin 0.5, vanillin 0.6, dehydrated alcohol 10.0, oil of lemon 20.0, oil of peppermint 3.0, cod-liver oil to 1000. The taste is covered but the odour persists to some extent.

**Oleum Jecoris cum Iodo.** *Syn.* OLIO DI FEGATO DI MERLUZZO IODATO (*P Ital V*). Contains 0.05% of iodine dissolved by trituration. *P Helv V* has 0.01%.

### **Emulsio Olei Morrhuæ (B.P.C.).**

*Dose*.— $\frac{1}{4}$  to 1 ounce (8 to 30 ml.). Contains 50% *v/v* of cod-liver oil.

### **Emulsum Olei Morrhuæ (U.S.P. XI)**

*Average dose* (3 times daily).—Infants, 2 drachms (8 ml.), adults,  $\frac{1}{2}$  ounce (15 ml.).

Cod-liver oil 50%, with acacia and syrup and 0.4% of methyl salicylate, or not more than 1% of any other flavouring agent prepared with recognised substances. Agar, gelatin, tragacanth or mixture of these may be used instead of acacia, and if the emulsion is stored 7% of water should be replaced by alcohol.

### **Emulsio Olei Morrhuæ et Creosoti (B.P.C.)**

*Dose*.— $\frac{1}{4}$  to 1 ounce (8 to 30 ml.). Contains 33 $\frac{1}{3}$ % *v/v* of cod-liver oil with 4 m. of creosote per oz.

**Emulsio Olei Jecoris Ferrata** (*P. Suec. A*) has cod-liver oil 300, calcium hypophosphite 6, citric acid 2, iron pyrophosphate with ammonium citrate 9, acacie 53, syrup 60, vanillin 0.6, dissolved in dilute alcohol 5 and water to 600.

**Ferrated Emulsion of Cod-Liver Oil** consists of the plain emulsion with iron and ammonium citrate 5 gr. per oz.

### **Emulsion of Cod-Liver Oil with Glycerophosphates, v p 41**

### **Emulsio Olei Morrhuæ cum Hypophosphitibus (B.P.C.)**

*Syn.* EMULSIO OLEI MORRHUÆ COMPOSITA

*Dose*.— $\frac{1}{4}$  to 1 ounce (8 to 30 ml.).

Cod-liver oil 50% *v/v* with 1 gr. each of sodium and calcium hypophosphites per dr.

**Emulsio Olei Morrhuæ cum Ovolecithino** is the above with 5 gr. of lecithin per oz. *Dose*.—2 to 8 drachms (7 to 30 ml.).

**Unguentum Zinci Morrhuatilis (B.P.C.).** Contains about 14% of cod-liver oil, with zinc oxide, talc, and balsam of Peru in a basis of wool fat, solution of calcium hydroxide, beeswax and soft paraffin.

**Cod-Vitamin** (Lilly, London). Cod-liver oil 40%, vitamin B extract 40%, malt extract 10%, potassium hypophosphite 1.7% with chocolate and aromatics 1 oz. contains vitamin A 5500 units, B 18 units, D 1300 units.

**Cybbiase** (Bengal, London). Drops containing cod-liver oil extract 40 g. and excipient to 100 g. 25 drops = 4 oz. of cod-liver oil. *Dose*.—For adults, 25 to 40 m. twice daily before meals.

**Desitin** (*Coates & Cooper, London*). Preparation of cod-liver oil for external use. Supplied as ointment or dusting powder for the treatment of burns, eczema, wounds, etc.

**Morelix** (*Gale, Buss, London*) A combination of cod-liver oil with malt, hypophosphites, Virginian prune, and aromatics. A nutritious tonic

**Morquette Cod-liver Oil Tablets** (*A H Cox, Brighton*) contain vitamin A, cholesterol and lipochrome-containing bodies, also phosphorus, bromine and iodine.

**Reinforced Cod Liver Oil** (*Pharmaceutical Specialities (May & Baker) Ltd., London*). Contains per ml 2000 i.u. of vitamin A and 500 i.u. of vitamin D.

### **Sodii Morrhuas** (*B.P.C.*).

**Dose.**—*Subcutaneously*  $\frac{1}{2}$  ml of a 3% solution slightly increased up to 2 ml., 2 or 3 times a week until reaction (febrile and local) occurs. When 2 ml has been reached give this dose *intramuscularly* up to 4 ml.

For *intravenous* use as a sclerosing agent, *v. postea*.

Sodium morrhuate consists of the sodium salts of the acids or of a fraction of the acids of cod-liver oil, usually purified by means of ether. The 10% *w/v* aqueous solution should be clear. The separated acids usually have m.p. 15° to 19°

Sodium morrhuate is a by-product from the manufacture of vitamin concentrates—S Caspe, *Indust Engng Chem*, 1933, 25, 1177

**Uses.** Sodium morrhuate was originally used in the treatment of leprosy. It has also been administered by injection in the treatment of lupus and tuberculosis. For these purposes the 3% solution is used. It is now used chiefly as a sclerosing agent in the injection treatment of varicose veins. In most cases a 5% solution of sodium morrhuate is strong enough to obliterate the lumen with a minimum amount of inflammation. It causes strictly localised mild inflammation of the vein wall, followed by firm fibrous occlusion of the vessel. The size of the vein is the determining factor as to the dosage. In small or medium-sized veins 1 or 2 ml is sufficient, while in large veins 3 to 5 ml is necessary. The total dose should not exceed 10 ml.

**Method of Administration.** Sodium morrhuate appears to be most effective when injected into a not fully distended vein, the patient is therefore best treated in a horizontal position by elevating the limb, and then applying digital pressure or a tourniquet above the point of injection. The standing position may be of advantage in the treatment of smaller veins. The effect on the injected vein is usually prompt. A few minutes after the injection the vein begins to harden below the site of injection for about 2 to 4 inches. Injections are given at 24 to 48-hour intervals, according to the response of the patient to the drug.

**GANGLIA** treated by sodium morrhuate injections 5%, 0.2 to 5 ml, after aspiration—Peter McEvedy, *Lancet*, 11/1930, 902.

**HÆMORRHOIDS** injected with sodium morrhuate.—A. S. Ross, *Brit. Med. J.*, 11/1930, 86.

**HYDROCELES**, providing they are primary and have not been caused by some lesion of the testicle, react well to aspiration and subsequent injection of 2 ml of a 5% solution of sodium morrhuate—David Levi, *Practitioner*, 1/1931, 506

**LEPROSY.**—Improvement in 2 or 3 cases after 2 or 3 injections of sodium morrhuate.—W. W. Cadbury, per *Trop Dis Bull*, 1921, 279.

**LUPUS**—3% solution intramuscularly, beginning with 0.5 ml increased to 3 ml gave striking results—the lesions completely involuted in 4 months.—*Brit med J Epit*, 1/1929, 98 See also Sir L. Rogers, *Brit med J*, 1/1921, 640

**VARICOSE VEINS** As a rule, except in the largest veins, there is no reaction or pain, and the swellings which may arise are diminished or gone within a week. In cases where there is no immediate result, further treatment is delayed for a month, when the veins usually become occluded or diminished in size—in the latter case an injection of 10% solution usually obliterates the veins.—P. B. Kittel, "Hæmodynamics," 1929

Sodium morrhuate 10% found more suitable than 5% (2 ml average for each injection). The latter will do for small veins. Patient seated in chair and no constricting bandage for at least 3 hours after injection. Less toxic than quinine-urethane.—F. A. E. Silcock, *Brit med J*, 11/1930, 303

The most popular injection for varicose veins at St. Mary's Hospital is a 5% solution of sodium morrhuate in 0.5% phenol, 13,000 ml of this solution was made during 1935.—C. M. Wilson, *Practitioner*, 1/1936, 653

Sodium morrhuate is definitely dangerous for intravenous injection. A case of sudden death in an elderly woman has been reported following injection of 2 ml., and other fatalities are reported in the literature.—David Levi, *Practitioner*, 1/1936, 506

Sodium morrhuate for veins not entirely free from danger.—A. H. Winchester, *Brit med J*, 11/1930, 120. Urticariiform wheals with pain for a week.—T. H. Treves-Barber, *ibid*, 60, 195

Sodium morrhuate thought to lead at times to immediate thrombus formation.—Reginald Payne, *Brit med J*, 1/1942, 237

### Injectio Sodii Morrhuatidis (B P C)

**Dose**—8 to 75 minims (0.5 to 5 ml.) intravenously 5% w/v.

**Episol** (Crookes Laboratories, London) Sodium morrhuate solution with sodium chloride 20%. Contains also 0.15% of a resinous compound from cod-liver oil. In varicose veins

Safest and most effective 0.5 to 2 ml obliterates from 3 to 30 cm. of vein. Normal dose for a vein 5 ml., and up to 30 ml given at one sitting. Relatively slight pain.—T. H. Treves-Barber, *Brit med J*, 1/1932, 143

**Sterules Sodium Morrhuate** (Martindale, London) contain  $\frac{1}{4}$ , 1 or 2 ml of 3% solution, also 2 ml of 5 and 10% solution.

**Varicane** (Pharmaceutical Specialities (May & Baker) Ltd, London) Solution of sodium morrhuate 5% and 10% for varicose vein injection

See also quinine and urethane, sodium chloride, and sodium salicylate for other sclerosing agents for varicose veins.

**Calciferol** (B P. Add)  $C_{28}H_{43}OH = 396.3$  Prop Name RADIOSOL (British Drug Houses, London)

**Dose**—Prophylactic (daily) for an infant  $\frac{1}{8}$  to  $\frac{1}{4}$  grain (0.025 to 0.05 mg.), equivalent to 1000 to 2000 units. Therapeutic (daily) for an infant  $\frac{1}{4}$  to  $\frac{3}{8}$  grain (0.05 to 0.075 mg.), equivalent to 2000 to 3000 units

Calciferol is pure vitamin D, possessing a potency of 40,000 i.u. per mg. It occurs in colourless, odourless crystals insoluble in water, soluble in alcohol 95%, ether, chloroform, acetone and vegetable oils. M.p. *in vacuo* 115° to 119°. It is prepared by the ultraviolet irradiation of ergosterol in a suitable solvent and separated from other products of irradiation by means of its 3:5-dinitrobenzoate

For full details of the chemistry, assay, and therapeutic uses of calciferol see Vol II. The following are additional references.

Vitamin D is recognised as a specific in the treatment of infantile rickets, spasmophilia and osteomalacia, diseases which are manifestations of abnormal calcium and phosphorus metabolism. Vitamin D is valuable in the preventive as well as curative treatment of these diseases. Complications such as certain renal diseases or glandular malfunction may preclude normal response to vitamin D therapy. During acute infections, especially of the gastro-intestinal tract, vitamin D may prove ineffective because poorly absorbed. Direct exposure of the skin to ultraviolet light from the sun or from artificial sources results in the formation of vitamin D within the organism, but the Council cannot recognise statements or implications that vitamin D has all beneficial effects of exposure to sunshine. There is clinical evidence to justify the statement that vitamin D plays an important role in tooth formation and maintenance of normal tooth structure, but there is no warrant for the claim that adequate vitamin D intake will ensure normal tooth structure or that adequate vitamin D will prevent dental caries. The vitamin D requirement is greatest during the period of infancy. Beyond the age of infancy the exact vitamin D requirement of man under any specified conditions is not known, but it appears that the requirement during pregnancy and lactation is increased.—Council on Pharmacy and Chemistry of A.M.A., *J. Amer. med. Ass.*, 1/1936, 1733

Bread containing the vitamin D equivalent of 3 dr. of cod-liver oil (in the form of irradiated ergosterol dissolved in corn oil) in the 24-ounce loaf now produced in 15 cities in Canada and 60 cities in the U.S.A. It is inconceivable that a vitamin so essential in the early years should not be essential throughout childhood and adult life—A. Brown and F. F. Tisdall, *Brit. med. J.*, 1/1933, 57.

ECZEMA.—In a group of eczema cases of both endogenous and exogenous origin, it was shown that the administration, in large doses, of vitamin D and a mixture of vitamins A and D proved useful in the great majority of cases. It accelerated the recovery, and the results were equally good in cases of internal and external origin. The treatment was more efficacious in young subjects and where there was an absence of endocrine disturbances—M. Comel, per *Brit. J. Dermat.*, 1935, 47, 490.

HYPERVITAMINOSIS D.—Toxic action due to (a) an unknown toxic substance, which causes arteriosclerosis, and (b) excess of vitamin D, which produces urinary calculi and retards growth. A diet of bread and milk protects against (a) but not against (b).—*J. Pharmacol.*, Nov., 1930, 371.

Different species of animals vary markedly in resistance to excess dosage. Whereas toxic effects in rats only occur after giving several thousand times the therapeutic dose, in dogs 20 times the curative dose causes death. The human subject may share this high susceptibility with the dog and clinical evidence points that way.—*Brit. med. J.*, 11/1931, 352.

Sheep, goats, rabbits, and guinea-pigs were fed on a "synthetic" diet, consisting essentially of regenerated cellulose, starch, sucrose, yeast, salts, and lard, with cod-liver oil. Sheep were reared successfully, goats with moderate success, but rabbits and guinea-pigs with much less success. Eventual failure in the last-named animals, and to a less extent in goats, was caused by the development of paralysis due to degeneration of the skeletal muscles, fatty liver being a constant finding in all species. It was demonstrated that the cod-liver oil was the chief causative agent in the production of the lesions. For sheep and goats a daily intake of 0.7 g. of oil per kg. of live weight caused death within 93 days, 0.35 g. within 226 days, and only when the oil ration was reduced to 0.1 g. was no ill effect produced.—Per R. T. Hewlett, *Lancet*, 1/1936, 115.

A fatal case of hypervitaminosis D in a baby of 11½ months. Young infants may have idiosyncrasy to the vitamin D contained in cod-liver oil as well as to artificially prepared calciferol. The present-day tendency to increase the

vitamin D potency of cod-liver oil is undesirable and unnecessary, that to which the public is accustomed, and upon which popular dosage is based—viz., about 100 i.u. per g.—is sufficient for all purposes. There is no reason whatever to administer cod-liver oil to infants during the summer months when diet and hygienic conditions are satisfactory and there is no evidence of rickets.—L. Thatcher, *Lancet*, 1/1936, 20

### **Liquor Calciferolis (B.P. Add.).**

**Dose.**—Prophylactic dose for an infant, 5 to 10 m (0.3 to 0.6 ml.), equivalent to 1000 to 2000 i.u., daily, therapeutic dose for an infant 10 to 15 m. (0.6 to 1 ml.) equivalent to 2000 to 3000 i.u. daily.

A solution of calciferol in a suitable oil, such as arachis oil, containing 3000 i.u. per g. It replaces *Liquor Ergosterolis Irradiati* (B.P.) which was permitted to contain the other products of the irradiation, together with unchanged ergosterol, in addition to calciferol.

**Liquor Ergosterolis Irradiati (U.S.P. XI) Average dose.**—5 m. (0.3 ml.).

An irradiated solution of ergosterol in an edible vegetable oil containing not less than 10,000 U.S.P. units of vitamin D per g.

**A.T. 10 (Antitetanisches Präparat Nr. 10).** See also Vol II, 20th Edn., p. 390

Thus only substance, which is closely related to vitamin D and contains the products of irradiation of ergosterol, is almost as active when given by the mouth as when injected. It is very toxic when the normal dose is much exceeded. It seems to be capable of completely replacing the parathyroid hormone, although the pharmacological actions of the two are quite different. During more than four years in which it has been given to about 300 cases of tetany it has never proved inert, its administration being invariably followed by recovery without any serious ill effects.—T. Ekblom, per *Brit. med. J. Epit.*, 11/1935, 88

**TETANY**—Very encouraging results in the prevention and treatment of tetany. It is undoubtedly superior to earlier parathroid preparations, its administration by the mouth being remarkably effective. The drug should be continued even after the well-known signs of tetany have disappeared, otherwise they are apt to recur.—O. Winterstein, *Dtsch. med. Wschr.*, 1934, 1831

### **Selectively Irradiated Ergosterol.**

The clinical potencies of irradiated ergosterols are not as great as would be expected from comparative rat assays of these products and of cod-liver oil. It has been suggested that the discrepancies between the expected and the actual clinical potencies of irradiated ergosterols may have been accounted for in part by the fact that irradiation of ergosterol with the full ultraviolet of the quartz mercury arc produces a multiplicity of products. Some of these products are known to be inactive physiologically and others to be toxic without appreciable antirachitic activity. Irradiation with a properly selected range of wave-lengths is capable of transforming ergosterol almost completely into a fraction which is antirachitically active in high degree and which is not contaminated with degradative decomposition products.

A product of selective irradiation of ergosterol is now available. It is a vegetable oil solution of the antirachitic factor, the potency of which has been adjusted to 10,000 U.S.P. X (revised 1934) units per g. Clinical studies are at present under way, and others are planned, to establish the optimum dosages of viosterol-in-oil (Sperti process).—T. H. Rider, G. Sperti, G. P. Goodt and H. G. Cassidy, *J. Amer. med. Ass.*, 1/1936, 456.

**Irradiated Milk.** Milk which has been irradiated with ultraviolet light has been administered in the treatment of rickets. The cure is more quickly and economically established by irradiated milk than by various irradiated commercial preparations. May be of value also in disorders incidental to pregnancy and lactation, the climacteric, malnutrition, injuries and surgical disease of bone, and some forms of tuberculosis.—Chalmers Watson, T. Y. Finlay and J. B. King, *Lancet*, 11/1929, 704.



Milk ordinarily sold throughout the year contains almost no antirachitic vitamin, and a good sample of cod-liver oil contains from 5 to 1000 times as much antirachitic vitamin as current samples of irradiated milk. The latter vary enormously.—K. H. Coward, *Lancet*, 11/1929, 1090, 1103

The therapeutic results in rickets from irradiated milk are not simply due to vitamin D in it—Chalmers Watson, *Brit med J*, 1/1930, 261

Potency of treated milk increased nine times by exposure of 8 seconds. Can cure as well as prevent rickets—D. Nabarro and J. O. Hickman, *Lancet*, 1/1930, 127.

### Liquor Vitaminæ-A (B.P.C.)

*Dose*.—5000 to 50,000 units

A solution in arachis or other suitable vegetable oil of a concentrate of mammalian or other livers. It contains 60,000 units of vitamin A per gramme; a small amount of vitamin D may also be present.

For full details of the chemistry, assay and therapeutic uses of vitamin A see Vol. II. The following is an additional reference.—

Present indications are that vitamin A is an aid toward establishing the resistance of the body to infections in general only when there has been an exhaustion of body reserves of the vitamin and the ingestion of vitamin A is inadequate. It certainly has not been shown to be specific in the prevention of colds, influenza and such infections, nor has it been demonstrated that ingestion of vitamin A far in excess of that necessary for normal body function, and readily obtained from a properly selected diet, is an aid in preventing various types of infections. A deficiency of vitamin A results in a retardation of growth when body stores of the vitamin have been depleted, but it must be borne in mind that vitamin A is no more important in promoting growth than other food essentials. There is at the present time inadequate evidence to warrant the claim that the ingestion of sufficient vitamin A will prevent the formation of renal calculi in man.—Council on Pharmacy and Chemistry of A.M.A., *J. Amer. med. Ass.*, 1/1936, 1733.

### VITAMIN PREPARATIONS OF COMMERCE

**A-B-D Capsules** (*Abbott, Montreal, Pharmaceutical Products, London*)

Contain vitamins A, B<sub>1</sub>, B<sub>2</sub>, and D. Each capsule is equivalent to 3 dr. of cod-liver oil (U.S.P.), 1 oz. of yeast in B<sub>1</sub> potency and  $\frac{1}{4}$  oz. of yeast in B<sub>2</sub> potency.

**Abidon** (*Parke, Davis, London*). Preparation of vitamins A, B<sub>1</sub>, B<sub>2</sub>, and D, consisting of a vitamin B concentrate in fish-liver oil. One capsule contains the equivalent of 3 dr. of cod-liver oil, 10 oz. of milk (B<sub>1</sub>) and 3 oz. of orange juice (B<sub>2</sub>). *Dose*—1 to 3 daily.

**Adexolin** (*Glaxo Laboratories, London*). Vitamin concentrate, each ml. containing 12,000 i.u. of vitamin A and 2000 i.u. of vitamin D. Supplied in capsules containing 3 m., also as emulsion containing 16,000 i.u. of vitamin A and 2800 i.u. of vitamin D per oz.

**Advita** (*Trufood, London*). Preparation containing vitamins A and D with a blue value of 1250 and containing 1000 units of vitamin D per g. Administered in 2 m. capsules.

**Avoleum** (*British Drug Houses, London*). A concentrated preparation of vitamin A, without admixture of vitamin D, containing 30,000 i.u. per g. In liquid or capsules containing 3 m. *Dose*—3 to 9 minims daily.

**Calcydic** (*Allen & Hanburys, London*). Flavoured granules containing per dr. 7 $\frac{1}{2}$  gr. of dicalcium phosphate, 1500 i.u. of vitamin D, and 30 gr. of dextrose. *Dose*— $\frac{1}{2}$  to 2 drachms.

**Calsimil** (*British Drug Houses, London*) Tablets containing 5 gr. of calcium sodium lactate and 500 i.u. of vitamin D.

**Calsolact D** (*Allen & Hanburys, London*) Tablets containing  $7\frac{1}{2}$  gr. of calcium sodium lactate with 1000 units of vitamin D.

**Calvitone** (*Martindale, London*). Contains per oz. calcium acid phosphate 5 gr., iron and copper citrate 10 gr., sodium and manganese glycerophosphate 5 gr., vitamin A 16,000 units and vitamin D 800 units. *Dose*—2 teaspoonfuls repeated. General tonic.

**Davitamon** (*Organon Laboratories, London*). Vitamin preparations containing vitamins A and D or both. Davitamon A contains 15,000 blue units per ml., Davitamon D 5000 units, Davitamon A and D contains these quantities of both vitamins per ml. Davitamon tablets contain 500 units of D, 0.02 g. of reduced iron and 0.0002 g. of copper carbonate.

**Essogen** (*Trufood, London*) A vitamin A preparation with a blue value of 2000. Supplied in capsules of 2 m.

**G.L. Preparation-A** (*Glaxo Laboratories, London*). A vitamin A concentrate. Each ml. contains 72,000 i.u. and each 3-min capsule 13,000 i.u.

**Greenosan** (*Bencard, London*). (Known as Spinatin in Denmark.) Vegetable extracts in tablet form, each 0.3 g. tablet containing chlorophyll 0.003 g., organic iron 0.001 g., lecithin 0.003 g., iodine (combined) 0.005%, with Ca, Mn, Mg, Cu and K in natural organic combination, vitamin A 33 i.u., vitamin C about 27 i.u., and vitamins B<sub>1</sub>, B<sub>2</sub>, D and E. For all conditions due to hypovitaminosis. Stated to be markedly more effective than equal dosage of the vitamins given alone. **Laxative Greenosan Tablets** contain also extract of aloes  $\frac{1}{2}$  gr., dry extract of cascara  $\frac{1}{10}$  gr., phenolphthalein  $\frac{1}{10}$  gr.

**Irradex** (*Parke, Davis, London*) Liver oil containing vitamins A and D, vitamin B extract, iron and ammonium citrate, and manganese citrate in malt extract base. *Dose*— $\frac{1}{2}$  to 4 teaspoonfuls. Malnutrition and debility.

**Multivite** (*British Drug Houses, London*) Chocolate-coated pellets containing in standardised amounts vitamins A, B, C, and D.

**Ostelin Preparations** (*Glaxo Laboratories, London*) **LIQUID** A glycerin suspension of calciferol containing 5000 i.u. of vitamin D per ml. **TABLETS** Calcium glycerophosphate 2 gr., with 500 i.u. of vitamin D. **EMULSION** 2800 i.u. of vitamin D per oz. **Colloidal Calcium with Ostelin.** A preparation of vitamin D for injection containing per ml. 5000 i.u. of vitamin D and 0.5 mg. of colloidal calcium. For urticaria, angioneurotic oedema, chilblains and other allergic states, also for delayed union of fractures. *Dose*—1 ampoule (1 ml.) at 3-day intervals, or daily for delayed union.

**Ostocalcium** (*Glaxo Laboratories, London*) Tablets contain  $7\frac{1}{2}$  grains of calcium sodium lactate and 500 i.u. of calciferol. *Dose*—1 to 12 tablets daily.

**Planavit A** (*Pharmaceutical Specialities (May & Baker) Ltd., London*) Standardised solution of vitamin A, prepared from fish-liver oils and containing 25,000 i.u. per ml.

**Radiostol Solution** (*British Drug Houses, London*) A brand of Liquor Calciferolis. **Radiostol Pellets** contain calciferol equivalent to 3000 i.u. in each. A solution in liquid paraffin for external application in the treatment of wounds, etc., is also available.

**Radiostoleum** (*British Drug Houses, London*) Preparations of vitamins A and D. Liquid contains per g. 15,000 i.u. of vitamin A and 3000 i.u. of vitamin D. Capsules, 3 m., contain the equivalent of 6 m. of the liquid. A 10% emulsion is also available for administration to infants.

**Syrup Minadex** (*Glaxo Laboratories, London*) Each fl. oz. contains vitamin A 1600 i.u., vitamin D (calciferol) 2700 i.u., iron and ammonium citrate  $13\frac{1}{2}$  gr., calcium glycerophosphate 2 gr., potassium glycerophosphate  $\frac{1}{2}$  gr., sodium glycerophosphate  $\frac{1}{2}$  gr., manganese glycerophosphate  $\frac{1}{2}$  gr., copper sulphate  $\frac{1}{2}$  gr. *Dose*— $\frac{1}{2}$  to 2 teaspoonfuls thrice daily.

**Torost** (*Glaxo Laboratories, London*) Combination of vitamin B complex and D in tablets containing 10 gr. of yeast and 500 i.u. of vitamin D.

**Viozin Ung.** (*Glaxo Laboratories, London*). A preparation of calciferol (500 i.u. per g.) in arachis oil, with zinc oxide in a wool fat and paraffin base. Promotes healing of wounds and varicose ulcers.

**Vitmar** (*Vitmar Ltd., London*). *Dose*—An egg-spoonful after meals every day. Described as a food containing vitamins A, B, and C, suitable for backward and delicate children. It is stated to have a food value of 400 calories per 100 g.

**Oleum Hippoglossi (B.P.C.).**

*Dose.*—2 to 5 minims (0.12 to 0.3 ml.).

The oil obtained by solvent extraction from the dried liver of the halibut, *Hippoglossus hippoglossus*. It is a pale yellow oil with a slightly fishy odour and taste.

The oil is particularly rich in vitamin A, but the vitamin content of the natural oil varies widely (*for details see Vol. II*). For commercial purposes the oil is usually adjusted, by admixture with weaker oil or with a vegetable oil, to a definite vitamin A content, and vitamin D is added so that the content of this vitamin is not less than 60 times that of good cod-liver oil.

**Halibol** (*Allen & Hanburys, London*). Halibut-liver oil with irradiated ergosterol. Vitamin A, 40,000 i.u. per g.; vitamin D, 10,000 i.u. per g.

**Haliborange** is a mixture of Halibol and concentrated orange juice. *Dose*—From a teaspoonful to two tablespoonfuls daily, according to age.

**Haliver Oil** (*Abbott, Montreal, Pharmaceutical Products, London*). Halibut-liver oil with irradiated ergosterol, with vitamin D potency of 11,000 i.u. per g., and vitamin A potency from 100 to 125 times that of standard cod-liver oil.

**Haliverol** (*Parke, Davis, London*). Halibut-liver oil with added vitamin D. The vitamin D potency is stated to be 250 times, and the vitamin A potency 60 times, that of cod-liver oil. *Dose.*—3 to 5 minims three times a day. Children 5 to 10 minims daily. Also available in capsules.

**Hallivite** (*Scott & Bowne, London*). Halibut-liver oil in pills and liquid.

**Halycalcyne** (*British Colloids, London*). Halibut-liver oil with calcium phosphate. A useful adjunct in treatment of chilblains and for dental caries.

**Halycitrol** (*British Colloids, London*). Halibut-liver oil and orange juice.

**Vitapon** (*Parnes & Byrne, London*). Halibut-liver oil standardised to contain 35,000 i.u. of vitamin A and 7,500 i.u. of vitamin D per gramme. Supplied in perles, liquid or tablets. **Vitapon Co. Tablets** contain Vitapon  $\frac{1}{2}$  m., parathyroid  $\frac{1}{10}$  gr., and calcium glycerophosphate. **Vitapex** liquid contains 35,000 i.u. of vitamin A and no vitamin D.

**Oleum Percomorphum** (*Mead, Johnson, Evansville, Indiana, U.S.A.*) A mixture of the liver oils of various species of *percomorphi*, which is 100 times richer than cod-liver oil in vitamins A and D. Supplied in capsules and liquid.

**Crookes' Super-D Oil** (*British Colloids, London*). Natural fish oils from fish of the order Scombridæ, containing approximately 50,000 i.u. per g. of both vitamins A and D.

**Mutton Bird Oil**, the oil of the young sooty petrel, collected on the Stewart Island, south of New Zealand, has been advocated as a substitute for cod-liver oil in phthisis and bronchitis.

With a rachitogenic diet 2% of cod-liver oil could be replaced by 1% mutton bird oil. The latter was superior in growth promoting value but for bone calcification the cod-liver oil appeared to be more satisfactory. Mutton bird oil at the rate of  $\frac{1}{4}$ % failed to prevent rickets.—*Per Nutr. Abstr. Rev.*, Apl, 1936, 1151.

**OLEUM OLIVÆ**

*B.P., U.S.P. XI, P. Helv V, P. Dan.*

*Dose.*— $\frac{1}{2}$  to 1 ounce (15 to 30 ml.).

The oil expressed from the ripe fruit of *Olea europæa* (Oleaceæ).

Inferior brands are obtained by addition of the pulped fruit to boiling water and by fermentation processes. The *B.P.* requires an acid value of not more than 2.0, but permits the use of an oil having an acid value of not more than 6.0 in making official liniments, ointments and plasters.

**Uses.** Olive oil is a nutrient and has laxative properties (*vide infra*). Often gives relief to patients who have gall-stones. It is frequently used warmed to about 90°F as rectal injection, as much as 10 oz. at bedtime for constipation. In typhoid  $\frac{1}{2}$ -oz. doses *per os*, and a breakfast-cupful by the bowel daily give great relief.

In gastric ulcer, given by stomach tube if necessary, it may inhibit the secretion of hydrochloric acid. It can be given for long periods and is harmless.

In preparing emulsions of olive oil of low acid value for external use, *e.g.*, with lime water, a few drops of oleic acid may be necessary in order to produce sufficient calcium oleate to act as emulsifying agent.

Chronic colitis is treated with from 8 to 10 oz. of washed olive oil, warmed to 100°F, injected per rectum at low pressure and retained all night—injections should be continued nightly for a fortnight—*Lancet*, 11/1923, 1411

A tablespoonful flavoured with peppermint before meals of value in digestive disorders and heartburn—W Morrell Roberts, per *Lancet*, 1/1931, 537

### **Emulsio Olei Olivæ (B.P.C.)**

**Dose.**— $\frac{1}{4}$  to 1 ounce (8 to 30 ml.) Contains 50% of olive oil

**Enema Olei Olivæ (B.P.C.).** **Dose**—20 ounces (600 ml). 20% v/v in mucilage of starch Undiluted, 5 to 20 ounces (150 to 600 ml.)

**Emema Oleosum (L.H.)** Olive oil 4, soft soap 1, warm water 16

**Unguentum Aquosum (B.P.)**

Distilled water 24, borax 1, olive oil 50, with white beeswax and white soft paraffin

**Maltolive (Martindale, London)** **Dose**—2 to 4 drachms (8 to 16 ml)

A combination of olive oil and malt extract A nutrient in emaciated and wasting conditions and in colitis of children.

### **Oleum Maydis (U.S.P. XI) Syn. CORN OIL.**

The refined oil expressed from the germ of *Zea Mays* (Gramineæ). A light yellow oil slightly soluble in alcohol, miscible in all proportions with ether, chloroform, benzene and light petroleum. Sp. gr 0 914 to 0 921.

## **OLEUM RICINI**

*B.P., U.S.P. XI, P. Helv. V, P. Dan.*

**Dose.**—1 to 4 drachms (4 to 16 ml.). Doses of 1 fl ounce (30 ml.) are often administered. *U.S.P. XI* average dose 4 drachms

Expressed from seeds of *Ricinus communis* (Euphorbiaceæ). Soluble about 1 in 3 $\frac{1}{4}$  of alcohol 90%. Miscible with ether and glacial acetic acid. The seeds, but not the oil, contain the poisonous protein, ricin; the "press cake," therefore, is poisonous. The purgative action is due to the fatty acids, of which ricinoleic is a principal member.

**Pharmaceutical** oil, as distinct from soap-makers' and other industrial oil, does not deposit in cold weather.

**Ricin.** A vegetable toxin or toxalbumin, is tremendously potent. When small doses are injected hypodermically immunity is produced, antiricin being formed. This fact paved the way for the foundation of serum therapeutics.—*Pharm. J.*, 1/1915, 156.

Ricin has two biological functions—one toxic, and the other antigenic. Potassium permanganate, hydrogen peroxide (30%), ozone, chlorine, bromine

iodine and ultra-violet rays, all destroy the toxic properties without affecting the antigenic. Ricin partially oxidised by potassium permanganate, when injected into rabbits, developed in them so great an immunity against untreated ricin that after 2 or 3 weeks they were able to receive 100 to 120 times the normal lethal dose, and 0.25 ml. of serum from these rabbits protected mice against a fatal dose of ricin.—E. B. Carmichael, *J. Pharmacol.*, Mar., 1929, 193

**Flavouring.** Prescribed as *Oleum Ricini Aromaticum*, or with 2 dr. of *Tinctura Cardamomi Composita* to the ounce, or in capsules.

**Pharmacology.** It passes the stomach unchanged, on reaching the small intestine it is saponified by the alkaline pancreatic secretion, being converted into glycerin and ricinoleic acid. This acid is irritant to the intestine, thus increasing peristalsis. If the oil were given saponified the ricinoleic acid would cause irritation and produce vomiting.—D. Grieve, *Pharm. J.*, 11/1921, 490

**Uses.** A mild but effectual purgative rarely causing pain. It is rendered more efficacious when mixed with an equal quantity of glycerin. The oil rubbed on the breasts will often increase the flow of milk. Castor oil is a soothing application to the conjunctiva and allays irritation due to foreign bodies in the eye. It is also employed for making solutions of alkaloidal bases for ophthalmic purposes.

**Capsules of Castor Oil** contain  $\frac{1}{4}$  or 1 drachm

**Capsules of Castor Oil, Compound**, contain croton oil  $\frac{1}{4}$  m., with castor oil 8 m. **Dose**—One or two

Prolonged inhalation of the vapour of castor oil produces a purgative effect. It is generally known among flying officers that the fumes from rotary engines using pure castor oil as a lubricant keep the bowels open.—G. C. Macphree, *Brit. med. J.*, 11/1934, 1045.

**Emulsio Olei Ricini Aromatici (B.P.C.).**

**Dose.**—1 to 2 ounces (30 to 60 ml.) Contains 30% v/v of aromatic castor oil.

**Enema Olei Ricini (B.P.C.)**

**Dose.**—20 ounces (600 ml.) 10% v/v in 5% w/v aqueous soft-soap solution.

**Mistura Olei Ricini (B.P.C.)**

**Dose.**—1 to 2 ounces (30 to 60 ml.)

An emulsion containing 3 dr. of castor oil per oz.

**Oleum Ricini Aromaticum (B.P.C.)**

**Dose.**—1 to 8 drachms (4 to 30 ml.)

Castor oil flavoured with vanillin, saccharin, chloroform and oils of cinnamon, clove and pimento. Should be recently prepared

**Unguentum Olei Ricini Compositum (L.H.)** *Syn.* BURN OINTMENT

Zinc oxide 1, yellow soft paraffin 2, hydrous wool fat 2, castor oil 3

**Magnesii Ricinoleas.** **Dose.**—1 to 4 drachms (4 to 16 g.).

A white powder, employed in preparations known as castor oil powders, or pills.

As much as 50% of castor oil can be incorporated in this way, but the compound is not a soap. The oil is for the most part free.

**Sodii Ricinoleas.** *Prop. Name.* SORICIN (*W. S. Merrell, Cincinnati; Squire, London*).

The sodium salt of ricinoleic acid. A powerful detoxifying agent. Solution in water suitably flavoured is used as a mouth wash, and a paste of sodium ricinoleate 1 and white soft paraffin 3 is used in dentistry.

Sodium ricinoleate lowers surface tension and adsorbs bacterial toxins. Is used as an antiseptic. For oral use in the treatment of pyorrhœa, a 1 to 4% solution is used, the solution being syringed into pyorrhœal pockets and allowed to remain a few minutes. Is also of value in gingivitis and Vincent's angina.

Certain virulent strains of bacteria (e.g., *B. tularensis*, *B. pestis* and *Spirillum cholerae*) when immersed in solutions of sodium ricinoleate become avirulent. Further, certain bacterial suspensions clear on addition of small amounts—*Lancet*, 11/1930, 117

The antiseptic activity, although marked, is limited to certain bacteria. Intestinal bacilli are resistant to all soaps and are unaffected. Bacilli found in respiratory organs and in the buccal mucous membrane are susceptible. Meningococcus, Pfeiffer's bacillus, diphtheria bacillus, tubercle bacillus, and *Brucella abortus* are destroyed. Streptococci are rapidly killed but staphylococci are unaffected, as also are moulds and yeasts.—H. Violle, *C. R. Acad. Sci., Paris*, 1933, 197, 714

**ACUTE GINGIVITIS.** Trichloroacetic acid as a strong caustic leaves the gums in a weakened condition and liable to further infection. Sodium ricinoleate is better—probably acts by adsorption into the toxin molecule. Apply 33% of yellow variety, or 9% of white to the dried sockets. Follow with hot potassium chlorate and carbolic mouth wash.—J. Wheatley, *per Pharm. J.*, 11/1931, 227

**Jelopar** (*Research Products, London*) Nasal jelly containing sodium ricinoleate, menthol, hexylresorcin, rosettol and liquid and soft paraffin. In catarrh, etc. **Lodynic** is a preparation of similar composition for use as a nasal spray

### Sodii Sulphoricinas. *Syn* TURKEY RED OIL.



Prepared by the action in the cold (not exceeding 50°) of sulphuric acid 1, on castor oil 3, washing with plenty of water and nearly neutralising the product with soda.

Concentrated solution of sodium sulphoricinate will dissolve iodine, resorcinol and naphthalene, forming strongly antiseptic solutions. It was employed as a glycerin substitute in the war

[P2] **Phenol Sodio-Sulphoricinate.** A mixture of phenol 1, and sodium sulphoricinate 4. A thick syrup miscible with water. 20 to 50% solution has been used for papilloma and tuberculosis of larynx and for ozæna.

Pharyngo-keratosis (mycosis) has been treated with 10% solution, also 10% solution of salicylic acid in the sulphoricinate.

**Ethidol** (*Burroughs Wellcome, London*). Ethyl iodoricinoleate, a stainless, non-irritating compound containing 20% of I. Used by injection or spread on dressing in all cases in which the application of iodine is indicated.

[P1] **Oleum Crotonis** (*B. P. C., P. Helv. V, Fr. Cx.*). *Syn.* OLEUM TIGLII.

[P1] "*Croton, oil of*"

**Dose.**— $\frac{1}{2}$  to 1 minim (0.03 to 0.06 ml.). *Fr. Cx.* gives max. during 24 hours 0.1 g. (= 2 minims nearly). Expressed from seeds of *Croton Tiglium* (Euphorbiaceæ). A yellow to brownish viscid liquid with nauseating odour and acrid taste.

**Soluble** in ether and in olive oil. Activity is due to croton-resin, a powerful irritant and vesicant.

**Antidotes.** Empty stomach by emetic or stomach tube. Keep patient lying down and warm. Give demulcent drinks freely. Stimulants, e.g., brandy  $\frac{1}{2}$  oz., or aromatic spirit of ammonia  $\frac{1}{2}$  dr.,

in water; spirit of camphor, 10 m. in milk, repeated. Tincture of opium by mouth to check the diarrhœa and relieve pain. Saline infusion.

**Uses.** The oil is a powerful skin irritant; it will blister and even cause suppuration and scarring. Internally it is so violent a purgative that it is rarely given except to lunatics for obstinate constipation, and in cases of apoplexy (1 or 2 drops placed on the back of the tongue). May be given as compound castor oil capsules, *q.v.*

[P1] **Linimentum Crotonis** (B.P.C.) contains 12% *v/v* of the oil with oil of cajuput and alcohol 90%

Well diluted may stimulate growth of hair on bald patches. Also used as a counter-irritant, but may produce powerful inflammation. In pneumonia of great benefit.

**ACUTE RHEUMATISM.**—Paint the muscular parts of the body near the affected joints with a mixture of equal parts of croton oil and blistering liquid using a rather stiff brush. A pustular and erythematous rash develops in about forty-eight hours, but is sometimes delayed to seventy-two hours. The effects of the rash are that the febrile temperature drops to normal, and the pain and swelling disappear. If one painting is not sufficient, paint again in a contiguous part (not the same), and so on. Most cases are completely cured by three paintings. It is shock therapy, but the shock is small and leads to no ill results. No medicine is necessary, especially not salicylates.—*Med Pr*, 1936, 191

[P1 S1] **Oleum Crotonis Compositum.** Mix blistering liquid 6 dr and almond oil 1 oz. Allow acetone to evaporate and add croton oil 40 m. Used as a paint once a week in whooping-cough—a success.—W J Midelton, *Brit med J.*, i/1923, 746.

**ABOR ARROW POISON** is believed to be a paste made by pounding the soft parts of *Croton Tiglium*: refs., 17th Edn

**Oleum Elliott**, so-called to distinguish from croton oil, is obtained from the seeds of *Croton Elliottanus*. Dose—1 to 3 minims, in capsules. A potent aperient

## OPIMUM

**Syn.** HUMBERGUM, TABAIACO, THEBAIACUM, SUCCUS PAPAVERIS SOMNIFERI CAPSULÆ INSPISSATUS (*The latter, contracted SUCC PAPAVERIS INSPISS. is occasionally used in prescriptions*). PULV. SUCC PAPAVERIS will denote Powdered Opium

[D] “Raw Opium (see p. 1023); prepared opium (see p. 1023), medicinal opium”

**NOTE**—*The Dangerous Drugs Act, 1925, section 4 (1) defines medicinal opium as raw opium which has undergone the processes necessary to adapt it for medicinal use in accordance with the requirements of the British Pharmacopœia, whether it is in the form of powder or is granulated or is in any other form, and whether it is or is not mixed with neutral substances.*

[P1] “Opium.”

[S1] “Opium except substances containing less than 0.2% of morphine calculated as anhydrous morphine.”

See also Morphine

The inspissated juice obtained by incision of the capsules of *Papaver somniferum* (Papaveraceæ). Only the Turkey and European varieties are allowed by the B.P. description. U.S.P. XI allows *P. somniferum* or its variety *album*. The Turkey product is best suited for pharmacy. Persian and Indian contain a large proportion of narcotine. The B.P. requires opium in its moist state, as imported, to contain not less than 9.5% of anhydrous morphine. When Opium is prescribed Opium Pulveratum must be dispensed. Fr. Cx requires 10 to 11% of morphine on the drug dried at 60°. I.A. requires 10%.

Opium (U.S.P. XI) in its normal moist condition contains not less than 9.5% of anhydrous morphine

**Incompatible** with vegetable astringents, alkaline carbonates, salts of mercury, iron, lead and zinc

**Antidotes.** Treat as for poisoning by morphine, see p. 638.

**Uses.** The oldest and most certain remedy for pain, also tends to check inflammation and relieve nervous diseases; lessens cough, arrests diarrhoea and dysentery (but is not advised for cholera). Children are very susceptible to its action. Externally the liniment is used for rheumatism, neuralgia and sciatica and is added to fomentations, but the addition of opium to preparations applied externally in this way is stated to be useless. As an ointment, e.g., with gall, it is applied to piles and fissures of the anus.

It relieves the pain in appendicitis but must not be given for this, as, apart from the danger of the symptoms being masked, opium may paralyse the intestines and cause tympanites.

"STAGE FRIGHT" may be treated with 5 to 10 drops of the tincture

LOOSENESS OF BOWELS is well treated by laudanum. In colitis where tenesmus is distressing, and stools contain blood and mucus, supplement dose by mouth by rectal injections (2 to 5 m. for a child) with a few grains of powdered ipecacuanha in  $\frac{1}{2}$  oz. of thin boiled starch.

### Opium Addiction.

For earlier references, including those to Opium Conferences under the League of Nations, see Vol. I, 20th Edn., pp. 623-4.

CONFERENCE ON LIMITATION OF MANUFACTURE (London, 1930). If each producing nation were allowed the quantity its manufacturers deem appropriate the total would greatly exceed the world's needs. League of Nations advised that 250 tons of raw opium and 6 tons of cocaine suffice for the world's requirements. Turkish statistics suggest that large quantities of opium, morphine, and heroin pass from its factories into illicit channels—in the first 6 months of 1930 2282 kg. of morphine and 4383 kg. of heroin were exported (the last amount represents 40 times the amount consumed in Gt. Britain in a year). Russia considers production of raw opium and coca leaf should be limited. Progress in suppression of use of narcotic drugs very slow—amazing that action on lines prescribed by our own Dangerous Drugs Acts has not been more widely adopted.—*Brit. med. J.*, ii/1930, 535, 572, 1084; i/1931, 1125.

OPIUM HABIT IN INDIA.—The habit of eating opium has no direct relationship with crime and is not socially objected to in India, provided excessive doses are not indulged in, but opium smoking is universally condemned. There is every reason to believe that the opium habit either inhibits impulses of a violent nature by lowering the vitality and reducing ambition and courage. When taken habitually in large doses for prolonged periods opium very seriously injures the physical and mental faculties of the addict. It does not, however, lead to



insanity. The average daily dose in a series of 1070 worked out at 10 grains.—R. N. Chopra and G. S. Chopra, *Indian J. med. Res.*, 1935, 388.

**OPIMUM HABIT IN CHINA.**—The efforts in China to stamp out the drug evil are by far the most drastic of any country in the world. In 1934 the death penalty was inflicted on 263 persons, mostly traffickers and manufacturers. Compulsory treatment is being enforced in 1935 in all detected cases of drug addiction and in 1936 any further drug addicts will not only have to undergo treatment but five years imprisonment as well. From 1937 onwards death or imprisonment for life will in all cases be inflicted for the non-medical use of manufactured drugs. There are now no less than 597 hospitals in China for the treatment of drug addiction and this number will be increased. It is claimed that 81,000 smokers and drug addicts were cured during the past year.—Report of Advisory Committee of the League of Nations on Traffic in Opium and other Dangerous Drugs, 1935

[P1-81] **Emplastrum Opii** (B.P. 1898). 1 in 10 of resin plaster (*exempt* [D]). [D P1 81] *Fr. Cx.* has opium extract 1, elemi 1, diachylon) plaster (*Fr. Cx.*) 2.

[P1] **Enema Opii** (B.P.C.) *Dose.*—2 to 4 ounces (60 to 120 ml)  
Tincture of opium 0.5 to 6% *v/v* in mucilage of starch.

[D-P1 81] **Extractum Opii Liquidum** (B.P.C.)

*Dose.*—5 to 30 minims (0.3 to 2 ml)

Contains 0.75% *w/v* of morphine.

[D-P1-81] **Extractum Opii Siccum** (B.P.) *Syn.* EXTRACTUM OPII AQUOSUM (*I.A.*), EXTRACTUM OPII (*P. Austr.*, *P. Helv.* V, *P. Belg.* IV, *P. Hung.*, *P.G.* VI, *P. Ned.* V, *P. Ital.* V, *F.E.* VIII).

*Dose.*— $\frac{1}{2}$  to 1 grain (0.016 to 0.06 g). 1 grain contains  $\frac{1}{8}$  grain of morphine. Standardised to 20% of morphine.

*Fr. Cx.* has the same with max. single dose  $1\frac{1}{2}$  grains, max. in 24 hours 5 grains approximately.

[P1] **Linctus Scillæ Compositus** (B.P.C.) *Syn.* LINCTUS SCILLÆ OPIATUS, GEE'S LINCTUS, LINCTUS CAMPHORÆ COMPOSITUS (*K.C.H.*, *P.E.H.C.* (not for children), *L.H.*, *St. G.H.*), LINCTUS SEDATIVUS (*St. T.H.*). *Dose.*— $\frac{1}{2}$  to 1 drachm (2 to 4 ml)

Camphorated tincture of opium, oxymel of squill, and syrup of tolu, equal parts.

[P1] **Linctus Tolu cum Opio** (*Brompton H.*) and **Linctus Scillæ et Tolu** (*W.H.*), *syn.* LINCTUS SCILLÆ CO., use syrup of squill in place of oxymel in preceding

[P1] **Linctus Opiatus** (*C.X.H.*). Tincture of opium 2 m., oxymel of squill 20 m., dilute sulphuric acid 5 m., treacle 20 m., water to 1 dr.

[P1] **Linctus Scillæ** (*St. M.H.*). Oxymel of squill  $\frac{1}{2}$  dr., camphorated tincture of opium 15 m., honey to 1 dr.

[P1] **Linctus Scillæ Compositus** (*U.C.H.*) contains oxymel of squill  $\frac{1}{2}$  dr., camphorated tincture of opium 10 m., tincture of ipecacuanha 5 m., mucilage of acacia to 1 dr.

[P1 81] **Linimentum Opii** (B.P.C.).

Tincture of opium 1, liniment of soap 1; filter after a few days (*exempt* [D]). An anodyne for pain.

[D-P1 81] **Liquor Opii Sedativus** (B.P.C.)

*Dose.*—5 to 30 minims (0.3 to 2 ml.).

Contains 1% *w/v* of anhydrous morphine, or about  $\frac{1}{4}$  grain in 30 minims.

[P1] **Mist. Acid. e. Opio** (N.I.F.).

Aromatic sulphuric acid 10 m, liquid extract of opium 5 m, water to  $\frac{1}{2}$  oz

[P1] **Mistura Opii et Glycyrrhizæ Composita** (U.S.P. XI) *Syn.* BROWN MIXTURE *Average dose*—1 drachm (4 ml)

Fluidextract of liquorice 12, potassium antimonytartrate 0.024, camphorated tincture of opium 12, spirit of ethyl nitrite 3, glycerin 12, in water to 100

[P1] **Mistura Sodæ cum Opio** (St M H) Tincture of opium 3 m, dilute hydrocyanic acid 2 m, sodium bicarbonate 6 gr, water to 1 oz

[D P1 81] **Opium Pulveratum** (B P, P Belg. IV, P. Ital. V, P. Helv. V) *Syn.* PULVIS OPII

*Dose*— $\frac{1}{2}$  to 3 grains (0.03 to 0.2 g.) 3 grains contains  $\frac{3}{8}$  grain of morphine.

Consists of opium dried at a moderate temperature, reduced to a fine or moderately fine powder and adjusted by the addition of lactose to contain 10% of anhydrous morphine.

U.S.P. XI includes **Opium Granulatum**, in No. 16 powder approx., and **Opium Pulveratum**, in very fine powder. Both contain 10 to 10.5% of anhydrous morphine

[D P1 81] **Pilulæ Saponis cum Opio** (B P C). *Syn.* PILULÆ SAPONIS COMPOSITÆ. *Dose.*—1 or 2 pills

Each pill contains  $\frac{1}{2}$  gr of powdered opium and about 1 gr. of hard soap.

[P1 81] **Pulvis Cretæ Aromaticus cum Opio** (B P.).

*Dose.*—10 to 60 grains (0.6 to 4 g) 60 grains contains about  $\frac{1}{2}$  gr of anhydrous morphine

Contains opium 2 $\frac{1}{2}$ % in Pulvis Cretæ Aromaticus (*exempt* [D]) Tablets each contain 5 grains (0.3 g)

[D P1 81] **Pulvis Opii Compositus** (B P C)

*Dose*—5 to 15 grains (0.3 to 1 g)

Contains 10% of powdered opium with black pepper, ginger, caraway and tragacanth.

*Note* Pulvis Opii Compositus (P. Ned. V) is Dover's powder

[P1] **Syrupus Camphoræ Compositus** (B V H) *Dose*—1 teaspoonful, containing tincture of opium about 1 m, vinegar of ipecacuanha 3 $\frac{1}{2}$  m, and vinegar of squill 1 $\frac{1}{2}$  m

Camphor 30 gr, oil of anise 30 m, benzoic acid 45 gr, glacial acetic acid 1 $\frac{1}{2}$  oz tincture of opium 2 $\frac{1}{2}$  oz, vinegar of squill 10 oz., vinegar of ipecacuanha 10 oz, sucrose 7 lb, burnt sugar q s, water to 1 gallon

[D P1 81] **Tinctura Opii** (B P) *Syn.* LAUDANUM, TINCTURA THEBAICA *Dose*—5 to 30 minims (0.3 to 2 ml). 30 minims contains  $\frac{1}{4}$  grain of morphine

Prepared by macerating opium in boiling distilled water to which alcohol is added after 6 hours. Contains 1% w/v of anhydrous morphine. P. Ned. V, P. Hung., P. Belg. IV and P. Ital. V contain 1% of morphine, made with 70% alcohol. P. Helv. V is made with 5% of extract of opium, using 20 of alcohol 95% and 70 of water. Fr. Cx and F.E. VIII dissolve 1 g. of opium extract in 19 g. of alcohol 70% to produce the same strength—*Max. single dose* 35 minims, max during 24 hours 110 minims approximately. I.A. requires 10% strength by percolation with alcohol 70% and 1% morphine.

[D-P1 81] **Tinctura Opii (U.S.P. XI)** *Syn.* TINCTURE OF DEODORIZED OPIUM. *Average dose.*—10 minims (0.6 ml.)

Granulated opium exhausted with water, the product evaporated, boiled for 15 minutes and allowed to stand overnight; the mixture is then heated to 80° and treated with hard paraffin; on cooling, the paraffin is removed and washed and the filtrate adjusted to volume with water, alcohol added and the product diluted with a mixture of alcohol and water so that the final tincture contains 1% of anhydrous morphine.

[P1] **Tinctura Anticholerica Conradi.** *Syn.* CONRAD'S KOLERADRAABER

*Dose.*—Over 20 years, 40 drops, over 5 years, 1 drop for each year. Must not be given to a child under 5 years

Tincture of opium 1, tincture of cascarrilla and camphorated spirit of ether, of each 2, bitter tincture of rhubarb 5

[P1] **Tinctura Thielemanni (P. Svec. X)** *Syn.* THIELEMANN'S KOLERA-DRAABER. *Dose.*— $\frac{1}{2}$  drachm (2 ml.).

Oil of peppermint 3, alcohol 90% 22, tincture of opium with saffron 10, tincture of ipecacuanha 25, ethereal tincture of valerian 40.

[P1] **Tinctura Opii Ammoniata (B.P.C.).** *Syn.* SCOTCH PAREGORIC. *Dose.*— $\frac{1}{2}$  to 1 drachm (2 to 4 ml.).

Contains 10% *v/v* of tincture of opium (equivalent to 0.1% of anhydrous morphine), 20% *v/v* of dilute solution of ammonia with oil of anise and benzoic acid. One ounce contains approximately  $\frac{1}{2}$  grain anhydrous morphine

[P1] **Gasman's Drops.** Liq. Ammon. Fort 10 m, Tinct. Capsici 10 m, Tinct. Opii 60 m Aq. Chlorof. ad 8 oz.—*Pharm. J.*, ii/1934, 595

[P1] **Tinctura Opii Camphorata (B.P.).** *Syn.* TINCTURA OPII BENZOICA (I.A.), TINCTURA CAMPHORÆ COMPOSITA, PAREGORIC, PAREGORIC ELIXIR, ELIXIR PARÉGORIQUE (Fr. Cx.).

*Dose.*— $\frac{1}{2}$  to 1 drachm (2 to 4 ml.). 1 drachm contains about  $\frac{1}{17}$  grain of anhydrous morphine

Tincture of opium 5% *v/v*, with benzoic acid, camphor and oil of anise in alcohol (60%). Contains 0.05% *w/v* of morphine.

P.G. VI, P. Belg. IV, F.E. VIII, and P. Ned. V have 0.05% of morphine, but amounts of the other ingredients differ. P. Jap. has 1 of opium in 200.

Tinct. Camph. Co. of the *Portuguese Pharmacopœia* is a [D P1 81] liniment containing 20 times as much opium as the British tincture.

[P1] **Tinctura Opii Camphorata (U.S.P. XI)** *Average dose.*—40 minims (4 ml.).

Tincture of opium 4, oil of anise 0.4, benzoic acid 0.4, camphor 0.4, glycerin 4, in sufficient diluted alcohol to produce 100. Strength 0.035 to 0.045% *w/v* of anhydrous morphine

[D-P1 81] **Tinctura Opii Crocata (B.P.C., I.A.).** *Syn.* SYDENHAM'S LAUDANUM. *Dose.*—5 to 30 minims (0.3 to 2 ml.).

Contains 1% *w/v* of anhydrous morphine (about  $\frac{1}{4}$  grain in 30 minims) with clove and cinnamon, and tinted with saffron.

P.G. VI, F.E. VIII, P. Belg. IV, P. Ned. V, P. Helv. V, Fr. Cx. *Supp.* 1920 approximate this.

[P1-81] **Tabellæ Pulveris Ipecacuanhæ et Opii (B.P.C.)** contain 5 gr (0.3 g.) (*exempt* [D]).

[P1] **Trochisci Sedativi (T.H.)** contain  $\frac{1}{2}$  gr of extract of opium with fruit basis.

[D P1-81] **Unguentum Opii.** 1 of extract in 10 of Unguentum Cetacei.

[D P I 81] *Vinum Opii Crocatum*, as used in Thielemann's Koleradraaber (g.v.), in Norway, has the composition—Opium powder 15, cinnamon 1, clove 1, saffron 5, Malaga wine 150

[D P I 81] *Koptalgos* (Duncan Flockhart, Edinburgh). Denarcotised preparation of opium containing 0.375% of morphine. Dose.—0.3 to 2.5 ml. in place of the tincture.

[D P I 81] *Liquor Opii Sedativus "Battley"* (Allen & Hanburys, London). A liquid preparation of opium containing 1 gr. of anhydrous morphine per dr. Dose.—5 to 10 minims.

[D P I 81] *Nepenthe* (Ferris, Bristol). A liquid preparation of opium containing 0.84% of anhydrous morphine (about 1 gr. in 130 minims)

[D P I 81] *Somnigen* (Hewlett, London). Dialysed solution of the hydrobromides of the alkaloids of opium in sherry, containing 0.75% w/v of anhydrous morphine. Dose.—5 to 40 m

[D P I 81] *Papaveretum* (B P C.). *Syn and Prop Names* OPIUM CONCENTRATUM (P.G. VI); ALOPON (Allen & Hanburys, London), in powder, oral tablets containing  $\frac{1}{2}$  gr. ( $\frac{1}{2}$  gr. morphine), 2% solution, ampoules containing  $\frac{1}{2}$  gr. or  $\frac{3}{4}$  gr., also supplied with atropine or hyoscine, OMNOPON (Hoffmann-La Roche, London) in oral tablets containing  $\frac{1}{2}$  gr., hypodermic tablets containing  $\frac{1}{2}$  gr., and in 1-ml. ampoules containing  $\frac{1}{2}$  gr., also in ampoules with hyoscine; OPOIDINE (Macfarlan, London) in tablets, hypodermic tablets and ampoules; PAVOPIN (T. & H. Smith, London)

Dose.— $\frac{1}{2}$  to  $\frac{3}{4}$  grain (0.01 to 0.02 g.);  $\frac{1}{2}$  to  $\frac{1}{4}$  grain (0.005 to 0.01 g.) by injection P G VI has max single dose  $\frac{1}{2}$  grain; max in 24 hours  $1\frac{1}{2}$  grains

The total or principal alkaloids of opium as hydrochlorides, adjusted to contain 50% morphine P G VI gives elaborate instructions for preparation

*Soluble* about 1 in 15 of water; less soluble in alcohol

Sahli expressed the opinion that the combined alkaloids would be the most effective narcotic. The effect of the morphine is considered to be enhanced by the presence of the other alkaloids, and the constipating action of opium is avoided

[D P I 81] *Tabellæ Papavereti* (B P C) contain  $\frac{1}{2}$  gr (0.01 g)

[D P I 81] *Hydrochlorates Alcaloideorum Principalium Opii* (P Ned V) *Syn* OPIALUM, OPIAL Dose—Max per os per diem 3 grains (0.2 g), 2 grains (0.12 g) by injection.

Contains narceine hydrochloride 1, thebaine hydrochloride 2, codeine hydrochloride 2.5, papaverine hydrochloride 4, narcotine hydrochloride 30, morphine hydrochloride 50, and sodium chloride 10.5%

[D P I 81] *Opiatum* (P. Helv. V) is similar, but contains 24.5% of narcotine hydrochloride and 66% of morphine hydrochloride, with no sodium chloride

There is less danger of toxic effects than from opium, as smaller quantities can be given—*Brit med. J.*, 11/1925, 804

Preferable to morphine as a sedative during first stage of labour. It may be administered orally or by injection in a dose of  $\frac{1}{2}$  gr., the injection being supplemented by 2 ml. of 50% solution of magnesium sulphate intramuscularly and repeated 2-hourly for two succeeding doses, according to Gwathmey's technique. Administration of morphine should be withheld until the cervix will admit three fingers, or the patient is not helped by potassium bromide and chloral hydrate.—L. McIlroy and H. Rodway, *J. Obstet. Gynec.*, 1933, 1175

[D P I 81] *Pavon* (Ciba, London). Total alkaloids of opium, containing 25% of morphine. Dose.— $\frac{1}{2}$  grain (1 tablet, 1 ampoule or 20 drops of 2% solution) 1 to 4 times a day

[P1] **Papaveris Capsula** (B.P.C., *P. Helv. V*). *Syn.* POPPY HEADS.

*Note.*—Fleurs de Coquelicot in France = poppy petals.

The dried fruits of *Papaver somniferum* before dehiscence has occurred. For making galenicals, the seeds are removed

[P1] **Decoctum Papaveris et Anthemidis Forte** (B.P.C.) *Syn.* DECOCTUM PAPAVERIS ET ANTHEMIDIS CONCENTRATUM

Contains 25% each of chamomile and poppy capsule in alcohol and water. Diluted with hot water it is used as a fomentation in neuralgia, peri-dental abscesses and gum-boils

[P1] **Extractum Papaveris Liquidum** (B.P.C.) *Syn.* LIQUOR PRO SYRUPO PAPAVERIS.

*Dose.*—10 to 30 minims (0.6 to 2 ml)

Contains about 0.17% of anhydrous morphine or about  $\frac{1}{2}$  gr in 30 m.

[P1] **Syrupus Papaveris** (B.P.C.)

*Dose.*— $\frac{1}{2}$  to 1 drachm (2 to 4 ml)

Liquid extract of poppy capsule 1 in 8 with syrup. Contains about  $\frac{1}{10}$  gr. of morphine per drachm

**Acidum Meconicum.**  $C_7H_4O_7 \cdot 3H_2O$  254.1 White crystals slightly soluble in water. A dicarboxylic hydroxy acid forming soluble salts with opium alkaloids. It occurs in good opium to extent of 5 to 8%. Has little physiological action.

**Rhæados Petalum** (B.P.C.). *Syn.* RED-POPPY PETALS.

The fresh or dried petals of *Papaver Rhæas* (Papaveraceæ)

**Syrupus Rhæados** (B.P.C.).

*Dose.*— $\frac{1}{2}$  to 1 drachm (2 to 4 ml). A solution of sucrose in an aqueous infusion of the dried petals. Used only as a colouring agent.

## OVOLCITHINUM

B.P.C

*Syn.* LECITHIN (*P. Ned V, F.F. VIII*)

*Dose.*—Internally 3 to 8 grains (0.2 to 0.5 g.) preferably half an hour before meals. This dose may well be increased if it is digested, as an average egg contains 16 gr. approx. Is usually administered as the elixir or in pills

Subcutaneously  $\frac{1}{4}$  to 2 grains (0.05 to 0.12 g.) in sterile olive oil every second day

A yellowish wax-like mass prepared from egg yolks by extraction with alcohol or ethyl acetate. When pure it consists of choline distearyl glycerophosphate, and is broken up by the pancreatic juice into glycerophosphoric acid, fatty acids and choline. It is a constituent of the brain 11%, and of yolk of egg 7%; milk (human, cows', etc.) contains varying amounts.

**Soluble** 1 in 30 of alcohol 90%, 1 in 5 of ether, and in chloroform, benzene, carbon disulphide and fatty oils. It combines with certain metals, e.g., copper.

**Uses.** When the phosphates excreted by the urine are high. Given in neurasthenia, various nervous diseases, diabetes, marasmus, tuberculosis, tabes and general paralysis; also in all diseases producing a disturbance of nutrition. It is said to cause a marked increase in patient's weight, to improve the general well-being, and to augment the blood corpuscles. In menorrhagia  $1\frac{1}{2}$  to 3 gr. of lecithin thrice daily between the periods has been found useful. Intramuscular injections of sterile oil solution have also given relief. Has given good results in myasthenia gravis. Cancer has been treated by  $2\frac{1}{2}$  gr lecithin injections.

**Elixir Ovolecithini** (*B.P.C.*) *Syn.* ELIXIR LECITHINI.

*Dose.*—1 to 4 drachms (4 to 16 ml.), half an hour before meals.

Contains 1 gr. of ovolecithin per dr. in a lemon-flavoured basis.

**Enema Ovi** (*B.P.C.*).

*Dose*—4 ounces (120 ml) 1 or 2 yolks of egg in peptonised beef tea.

[P 81] **Pilulæ Ovolecithini** (*B.P.C.*) *Syn.* PILULÆ LECITHINI.

*Dose*—1 to 4 pills. Contain  $\frac{1}{10}$  gr. of strychnine and  $1\frac{1}{2}$  gr. of ovolecithin.

**Bromlecithin** (*Richter, London*) Described as a natural lecithin, containing 20% of bromine in tablets of  $\frac{1}{2}$  gr. and 4 gr. For anæmia, neurasthenia and hysteria. *Dose*—1 to 2 tablets thrice daily.

**Iodolecithin** is a similar compound with 20% of iodine in place of bromine, in 4 gr. tablets and  $1\frac{1}{2}$  gr. pills for arteriosclerosis, rickets and asthma. *Dose*—1 tablet or 1 to 2 pills thrice daily.

**Lecithinol** (*Richter, London*) Solution of lecithin in olive oil, in ampoules, for administration in neurasthenia and malnutrition. *Dose*—1 ml. injected 3 or 4 times weekly.

**Promonta** (*Promonta, Hamburg, Pharmaceutical Products, London*) A "nerve-food" containing the active constituents of the substance of the central nervous system, cholesterin "in natural combination with the phosphatides of the brain substance," "albuminoids," vitamins A, B, D and E, "assimilable carbohydrates," calcium glycerophosphate, and iron. Prepared in powder or pastilles.

## OXYGENIUM

*B.P., U.S.P. XI, Fr. Cx.*

O = 16 000

Oxygen is obtained commercially by the rectification of liquid air by a process of fractional liquefaction, or by the electrolysis of water. It is of not less than 98% purity.

It is sold compressed in cylinders, a common size containing the equivalent of 20 cubic feet (560 litres approximately) for inhalation. It may be mixed with air at the time, or be passed direct into the patient's mouth by a glass tube or from a funnel above the face (the latter method is probably of little use—*vide infra*).

**Administration.** Warm the gas by discharging it into a rubber gas bag and keeping in same for an hour or two if possible prior to use. Open the cylinder in an adjoining room so as not to alarm the patient.

A hot-water box may contain a spiral metal tube, through which the oxygen passes to the patient from the bag. A Woulf's bottle containing hot water is also useful—the gas being bubbled through it.

**Uses.** Inhalation of oxygen is of great service in pneumonia, bronchitis, asthma, angina; it relieves dyspnoea, and reduces temperature. May be used after chloroform to accelerate recovery. It is the best cardiac and respiratory stimulant. Severe cases of whooping-cough have been treated—give just before onset if possible. In vomiting of phthisis it is said to have been effective. It has been used as an antidote to morphine, opium, strychnine, cyanide, nitrous oxide and carbon monoxide poisoning, and for resuscitation after partial drowning.

In hæmorrhage, anæmia, etc., of doubtful use. Airs of more than 60% of oxygen may produce pulmonary inflammation. Oxygen-enriched airs are of life-saving value in pulmonary obstruction, œdema, or other deficiencies retarding oxygen absorption or preventing full saturation of the hæmoglobin of the pulmonary blood. Must be used with care.—C. W. Greene, *J. Amer. med. Ass.*, ii/1925, 645.

In congenital heart disease oxygen is of no avail; not indicated in cyanosis of cardiac origin, when lungs are comparatively clear. Chronic cyanosis of emphysema is temporarily relieved. Specially called for in acute pulmonary failure, together with inadequate ability for compensation by the heart and blood. Should be administered over hours or days.—Per *J. Amer. med. Ass.*, ii/1925, 1430.

Indications for oxygen therapy.—W. T. Richie, *Brit. med. J.*, ii/1927, 915

Oxygen therapy.—W. M. Boothby (Council on Physical Therapy, A.M.A.), *J. Amer. med. Ass.*, ii/1932, 2026, 2106.

A mixture consisting of about  $\frac{1}{3}$  oxygen and  $\frac{2}{3}$  helium, administered by means of an air-tight oxygen tent with a specially designed hood just large enough for the head, is of definite value in relieving patients with severe intractable asthma. In status asthmaticus it can be life-saving. Its use may also be warranted in cases in which respiratory difficulty is so great that the cyanosis is not relieved by administration of 80% oxygen and 20% nitrogen. No ill-effects noted—one patient inhaled helium for nearly 24 hours continuously, and subsequently at intervals of 3 days. Effectiveness of helium believed due to its rapid diffusion.—C. K. Maytum, L. E. Prickman and W. M. Boothby, *Proc. Mayo Clin.*, 1935, 788.

**Injection of Oxygen.** Oxygen has been given by injection by various routes—endovenous, intraperitoneal, rectal and subcutaneous.

Endovenous injection of 120 ml. of oxygen slowly has been tried in the case of a patient *in extremis*.

**Subcutaneously**, oxygen has been given in sciatica in doses of 250 to 400 ml., injected deeply, and in asphyxia, pneumonia and tuberculosis.

Intraperitoneal injections are of value in tubercular diarrhoea, tubercular peritonitis and "tabes mesenterica."—R. S. Grewal, *Indian med Gaz.*, Sept., 1925, 421.

Rectal injections are of value in certain types of colitis. Growth of anaerobic bacteria is inhibited and the injured mucous membrane benefited.—J. A. Campbell, *Brit. med. J.*, ii/1932, 422.

Preferential site for injections is the outer border of the anterior surface of the thigh, three inches above the upper border of the patella. 150 to 500 ml. satisfactory. Valuable in neo-natal asphyxia, drowning, suffocation, carbon monoxide poisoning, lobar pneumonia, pleurisy, pulmonary tuberculosis, cardiac asthma, collapse due to hæmorrhage, and as a prophylactic of post-operative shock (500 ml. being injected at full pressure in 1 minute).—D. C. Welsh, *Brit. med. J.*, ii/1932, 147.

**HÆMOPTYSIS.** Brilliant results in 80% of 50 cases following injection of 600 to 1000 ml subcutaneously (site of injection not important) —A. Latunne, *Brux. méd.*, 1934, 219.

**TUBERCULAR HÆMOPTYSIS** treated by oxygen injected subcutaneously, 500 to 600 ml. under the skin of the chest, if possible on the affected side. In 12 out of 20 cases hæmorrhage stopped at once, and in 4 after the injection had been repeated daily for 3 or 4 days —A. Courcoux, per *Med. Annu.*, 1935, 453. Site of injection not important (may be given under skin of thigh), and smaller doses, e.g., 200 ml., are sufficient. —Pierre-Bourgeois, *ibid.*

**PNEUMONIA.** In pneumonia, as a preventive of chloroform or post-anæsthetic sickness, and in extensive burns and scalds. If sufficient is given to inflate an area of skin equal in size to the palms of two hands, the amount given is roughly 200 ml. In bad cases give at least 400 ml. and repeat in 6 hours if absorbed. The gas need not be heated or filtered, does not produce or aggravate lung trouble or cause local or general bad effects. Inject below and outside the nipple or breast. —T. S. Kirk, *Brit. med. J.*, ii/1928, 195.

**PULMONARY TUBERCULOSIS.** The injections, at a dosage of 200 ml. per injection, are given in the subcutaneous tissues of the anterolateral region of the thigh with an apparatus such as is commonly used for the performance of pneumothorax. The injections should be given slowly, and should be repeated every other day for about a month. The treatment results in disappearance of fever, increase of the blood pressure, improvement of the blood picture, formation of a greater number of erythrocytes and amelioration of the disease. —E. Frola, per *J. Amer. med. Ass.*, i/1936, 1430.

**Ozone.**  $O_3 = 48$

Is known as active or tri-atomic oxygen. It is a very powerful oxidising agent, the third atom of oxygen in the molecule being in the labile condition.

The effect of passing electrical currents through oxygen is to produce ozone, which may be recognised by the peculiar odour. When in large quantity it is irritating to the air passages, causing cough and headache. Mildly ozonised air has been inhaled for phthisis and the spasmodic stage of whooping-cough.

It has been suggested that inhalation of ozone is injurious to the respiratory tract rather than beneficial in warding off injurious diseases, but this is exaggerated.

**Octozone.** A concentrated and potent form of ozone, produced by passing oxygen at a pressure of 5 lb. through an electroniser in which it is subjected to a silent electrical discharge. True composition not yet definitely decided. It is soluble in water and if stored in glass containers retains its properties for some days. Perishes red surgical rubber in less than 30 seconds. Too pungent to be inhaled, but may be used externally in the form of a bath or as local application, or by intramuscular or rectal injection. Drinking it dissolved in water acts as gentle laxative. Has rapid action on wounds and ulcers, also in arthritis, neuritis, sciatica, etc. —O. Parkes and C. H. Buckley, *Lancet*, ii/1931, 849.

**Nitrogen.**  $N = 14.008$ . Nitrogen is a colourless, odourless, tasteless gas constituting about 77% by weight (79% by volume) of the atmosphere. Nitrogen prepared from the atmosphere contains a small amount of argon and other rare gases. 1 litre of nitrogen weighs 1.25072 g. at 0° and 760 mm. pressure. It is only slightly soluble in water.

### Artificial Pneumothorax.

This consists in introducing nitrogen or sterile air between the two layers of the pleura through a special needle, and thus inducing collapse of the lung. There is no chosen spot for the puncture—it is commonly made in one of the axillary lines in the seventh or eighth intercostal space. The aim is to find a spot where the lung is healthiest and to avoid the neighbourhood of cavities. A hypodermic injection of morphine is given  $\frac{1}{4}$  hour before the operation. A local anæsthetic such as 2% procaine hydrochloride is given to anæsthetise the body tissues down to the pleura.



The quantity of nitrogen or air injection is 200 to 300 ml. More may be given the 1st and 3rd days after the initial dose, and then subsequently at increasing intervals. Collapse may be maintained for 2 to 3 years or more.

Only those cases in which the disease is unilateral or mainly unilateral are suitable—a radiogram is essential. It is the exudative type of lesion, which looks soft in the X ray, that calls for the treatment. Apical lesions are not suitable. Rarely used in patients over 45. It is suitable in cases of spontaneous pneumothorax proved to be due to tuberculosis and may be used as an emergency measure in pulmonary hæmorrhage. It is unsuitable in tuberculous laryngitis, except when the lung disease is unilateral, also in intestinal tuberculosis. It is contraindicated in severe cardiovascular disease. It is urgently called for in pulmonary tuberculosis in pregnancy and is of value in diabetics developing the disease. On these lines it is a valuable form of treatment in 5% of all cases of pulmonary tuberculosis. Three years' treatment the average. The great danger is the supervention of a pyopneumothorax.—A. L. Punch, *Brit med J*, i/1934, 179.

This form of treatment is, or should be, available for suitable patients (5 to 10% at least) under the tuberculosis schemes of all local authorities. There should be careful selection of cases—in certain types collapse-therapy is unnecessary and sometimes harmful. The young adult with a unilateral lesion and no tubercle bacilli in the sputum, the young adult with slight early infiltration without cavitation, with good general condition and normal blood picture and who is ambulant and afebrile, the man over 45 with slight fresh infiltration superimposed on an old fibroid tuberculosis, and a patient with bilateral disease and low resistance—are all examples of cases in which routine treatment, including rest, is indicated, and in which as a rule artificial pneumothorax is not in itself a cure for tuberculosis any more than a splint heals a broken leg. It is a means for putting a body with a diseased lung into a favourable condition to develop healing and powers of natural resistance. Beneficial as are its results it demands expert technique, careful selection of cases and careful study of the individual patient. It is not a rule of thumb treatment to be prescribed on X-ray evidence alone.—*Rep. med. Offr. Minst. Hlth., Lond.*, 1933, 134.

Indications and contraindications.—L. S. T. Burrell, *Practitioner*, 11/1933, 392.

Highly satisfactory in the treatment of tuberculosis of the larynx. Of 35 cases, 24 were clinically cured or improved, in 6 the condition remained stationary and in 5 became worse.—R. Scott Stevenson, *Brit med J*, 11/1933, 962.

In lobar pneumonia a pneumothorax should be produced as early as possible. 400 to 500 ml. usually given with ease, and two injections suffice in most cases, given at an interval of 24 hours. Striking relief of pain and dyspnoea, but severity and not course of disease altered.—A. Behrend and R. B. G. Cowper, *J. Amer. med. Ass.*, 1/1934, 1907.

Pneumothorax treatment in France increases in popularity. Some 35,000 refills were given during 1934, but this is said not to represent the full extent of the practice.—*Per Brit med. J.*, 1/1936, 119.

For earlier references see previous editions.

**Nitrogenii Monoxidum (B.P., U.S.P. XI)**  $\text{N}_2\text{O} = 44.02$   
Syn. NITROUS OXIDE, LAUGHING GAS.

A colourless gas with characteristic odour and faintly sweetish taste. Soluble 1 in 2 (by volume) of water at ordinary temperatures.

Is prepared by heating ammonium nitrate to about  $180^\circ$  when it splits up into nitrous oxide and water vapour.

The gas is passed through a strong solution of ferrous sulphate to remove nitric oxide—the traces of acid being removed by passing through alkali. The gas is considered one of the safest anæsthetics. The heart is not directly affected by its action.

### TREATMENT IF DANGEROUS SYMPTOMS ARISE DURING ADMINISTRATION OF NITROUS OXIDE

Dangers arising under gas are almost invariably due to failure of the respiration caused either by obstruction or overdose. Obstruction may result from "falling back of the tongue," from pressure due to engorgement of the thyroid or thymus, or other glands, or from foreign bodies entering the respiratory passages—teeth, bloodclot, vomit, etc. Overdose is more likely to occur if the patient's clothing be not loose.

If the breathing stop, give no more anæsthetic, clear the mouth and pharynx with a swab or towel round the finger, pull forward the tongue and compress the lower ribs, if no air enters or leaves the chest, place the patient upon his side upon the floor, with a pillow or something equivalent under his shoulders. Loosen his clothing, pull the tongue forward and give the tongue forceps to an assistant to keep up the traction. Try to expel any possible obstruction by compressing the lower ribs and abdomen, and then turn the patient upon his back and begin artificial respiration, giving oxygen gas and applying amyl nitrite or weak ammonia vapour to the nostrils meanwhile. If there is another assistant tell him to give an injection of strychnine ( $\frac{1}{4}$  grain) or 1 drachm of ether or both, but do not stop the artificial respiration or waste time over the injection yourself. If no air enters or leaves the chest during the artificial respiration, do tracheotomy forthwith, and immediately the trachea is entered resume the artificial respiration and continue it for at least an hour, keeping the patient warm during this time.

It may be preferable, nitrous oxide being half as heavy again as air, to place the patient face downwards—in the "prone" position with a pad below the chest and the forehead upon the right forearm. Then press with the hands over the lower ribs and maintain this for 3 seconds. Then turn the patient on the right side, maintain that position also for 3 seconds—repeating these movements alternately. It may suffice simply to hold patient upside down.

**Uses.** Nitrous oxide is employed as an anæsthetic in minor surgery, in conjunction with oxygen as a general anæsthetic for major surgery and obstetrics, and for the induction of anæsthesia prior to maintenance with ether. Its advantages are that it is non-irritant, non-toxic, rapid in action, and recovery is equally rapid. Disadvantages are that unless oxygen or air is given, asphyxia occurs, while its effect is greatly reduced if more than minimal amounts of oxygen are admitted, muscular relaxation is poor, and blood pressure is increased. An additional disadvantage is the weight of the cylinders, which limits portability. As ordinarily administered *per se*, e.g., for dental extractions, anæsthesia is complete in about  $\frac{1}{2}$  minute, lasts for 20 to 40 seconds and recovery is usually complete in 2 to 3 minutes. Nitrous oxide is administered by means of a bag into which the gas is led from the cylinders, the bag communicating with the face-mask through a valve by which the expired gas is passed out into the air. Various forms of apparatus are also available by which the gas may be administered intranasally.

**Nitrous Oxide and Oxygen** has been extensively used for major surgery. Preliminary medication with hypnotics is utilised, since a higher proportion of oxygen may then be employed. Pure nitrous oxide is administered at first, oxygen being admitted after induction as required to prevent anoxæmia while maintaining a sufficient depth of anæsthesia. Anæsthesia with gas-oxygen is frequently supplemented by the administration of very small amounts of ether. With this addition heavy pre-operative medication may be avoided, thus lessening the risk of respiratory failure.

For operations on regions other than the mouth or nose, injections of atropine  $\frac{1}{10}$  to  $\frac{1}{5}$  gr., morphine  $\frac{1}{4}$  to  $\frac{1}{2}$  gr., are given hypodermically  $\frac{1}{4}$  or even 2 hours before the inhalation. Crile and others add scopolamine  $\frac{1}{10}$  to  $\frac{1}{15}$  grain. At first nitrous oxide with 2% oxygen is given with a pressure of 4 to 40 mm of mercury. More or less oxygen is given according to circumstances—more if patient is cyanosed, less if he struggles. Unconquerable rigidity is controlled by giving ether—this may occur in about 10% of cases.—D. W. Buxton's *Anæsthetics*, 6th Edition.

Nitrous oxide has been repeated on the same patient every day for more than a month without harmful effects. Satisfactory anæsthesia cannot be secured with nitrous oxide and oxygen except with adequate preparation; necessary for the patient to be receptive of the gas type of anæsthesia, i.e., with blood stream capable of receiving and using the gas supplied. Anæsthetist must know metabolism of patient.—F. H. McMechan, *Brit. med. J.*, ii/1926, 1118.

Surgical anæsthesia with nitrous oxide depends partly on the presence of a certain degree of anoxæmia, and this must impose a limitation on its uses and increase its dangers.—W. E. Brown and co-workers, *J. Pharmacol.*, 1927, 269.

Gas-oxygen an effective substitute for ether or chloroform. Contraindications—face and mouth operations: changes in colour render it unsuitable for endoscopic examination of mucosæ, and congestive bleeding may make some operations difficult. Apparatus rather expensive.—A. H. Macklin, *Lancet*, i/1930, 1231.

Nitrous oxide and oxygen better than ether alone in any case where it is important to prevent or minimise shock.—F. P. de Caux, *Brit. med. J.*, ii/1930, 81.

A portable gas and oxygen apparatus for use in obstetrics by general practitioners.—J. Elam, *Brit. med. J.*, ii/1933, 829.

During the second stage of labour, nitrous oxide gas and oxygen (ideal proportions 80 and 20%, but oxygen increased if co-operation is not good), administered by Boyle's or McKesson's portable apparatus, appear to give the best results. Duration, strength and frequency of uterine contraction increased rather than diminished in over 50% of cases investigated, and no instance of post-partum hæmorrhage. Administration of anæsthetic continued for half to three-quarters of a minute after each pain has ceased. During birth of the head chloroform should be added, but should be regarded only as an adjunct to nitrous oxide, and only used in sufficient quantity to relieve pain at the most acute stage.—L. McIlroy and H. Rodway, *J. Obst. Gynec.*, 1933, 1175.

The best modern anæsthetic. Best administered by the McKesson apparatus, without the use of ether or chloroform, and preceded by Omnopon and scopolamine as premedication. Ensures complete absence of psychic shock, is not followed by vomiting and does not aggravate any pathological condition present.—R. Jarman, *Brit. med. J.*, i/1934, 799.

## PANCREAS

The pancreatic juice of man contains several digestive ferments:—

Trypsin, a proteolytic enzyme acting in an alkaline medium, converting protein, e.g., casein of milk and fibrin, into peptones; amylase (amyllopsin) or pancreatic diastase which converts starch into dextrin, maltose and dextrose; lipase (steapsin), a lipolytic enzyme (emulsifies fats); and possibly the milk-curdling enzyme, rennin, converting casein into a form of peptone.

The idea that rennin is present in the pancreatic juice is not held by many (*vide* Bainbridge and Menzies, *Essentials of Physiology*) who consider that trypsin is the milk-curdling principle. The presence of rennin would seem to be unnecessary in view of the active milk-curdling property of the gastric juice.

For invalids, aged persons, and those suffering from weak digestion, or those prostrated by fever or exhaustion, preparations

of the pancreas of the pig (an omnivorous animal) may be employed, by means of which food may be partially or wholly digested previous to administration; their nutrition is thus maintained, and the stomach has time to regain its powers of digestion. The pancreas plays an important part in enabling the organism to resist infection, and the spleen is said to assist by producing a hormone which activates trypsinogen and raises the phagocytic index. Pancreatic juice, obtained in its inactive form from the pancreatic duct, acquires powerful proteolytic activity by mixing with it a soluble calcium salt and incubating.

**SPRUE.** Raw pancreas—initial dose a teaspoonful, increased to a tablespoonful of chopped mass, including juice, once or twice daily, useful adjuvant. —A. Castellani, *J. trop. Med. (Hyg)*, 1925, 231.

**Pancreatinum** (*B.P.*, *U.S.P. XI*, *Fr. Cx.*).

**Dose.**—3 to 10 grains (0.2 to 0.6 g.). *U.S.P. XI* average dose 8 grains. It should be given 2 to 3 hours after a meal to prevent its destruction by gastric acid.

A white or buff-coloured powder containing the enzymes trypsin, lipase and amylase, in respect of each of which the *B.P.* specifies a minimum standard of activity. It digests albuminoids and converts, if of *U.S.P.* standard, not less than 25 times its weight of starch into soluble carbohydrate.

It differs from pepsin in the rapid destruction of its proteolytic activity in the presence of acid.

**Soluble** in water, giving a turbid solution. Insoluble in alcohol 90% and in ether.

**Uses.** Aids the digestion of starch and protein, acting best in nearly neutral solution. Its activity is destroyed when solutions containing it are heated above 60°. Is used mainly for the preparation of pre-digested or peptonised foods (*vide infra*).

In chronic pancreatitis, pancreatin in suitable intestinal medication may be employed with advantage before the operation and also in cases unsuitable for operations.—Whitla.

**SPRUE.** Pancreatin in 5 to 10 g. doses with 20 to 40 g. of calcium carbonate, 3 times a day 2 hours after food, has been given with success. The treatment is based on results of experiments which showed complete absence of pancreatic ferment.—*Trop. Dis. Bull.*, 1921, 50

**Enema Pancreatini** (*B.P.C.*).

**Dose.**—4 ounces (120 ml.). Solution of pancreatin 6.5% *v/v* in equal parts of milk and beef tea.

**Glycerinum Pancreatini** (*B.P.C.*).

**Dose.**— $\frac{1}{2}$  to 1 drachm (2 to 4 ml.). 1 in 10.

**Liquor Pancreatini** (*B.P.C.*). *Syn.* LIQUOR PANCREATIS.

**Dose.**— $\frac{1}{2}$  to 2 drachms (2 to 8 ml.).

Contains 16 $\frac{1}{2}$ % *v/v* of glycerin of pancreatin with sodium bicarbonate in a diluted alcohol-glycerin solution.

**Pulvis Pancreatini Compositus** (*B.P.C.*). *Syn.* PULVIS PANCREATICUS, PEPTONISING POWDER.

Pancreatin 1, sodium bicarbonate 4.

Place the powder into a clean quart bottle with  $\frac{1}{2}$  pint of cool water, add a pint of fresh milk, and shake. Place the bottle in warm water for ten minutes, then pour the milk into a saucepan and heat quickly to boiling and allow to cool.

**Peptonised Milk.** To 25 gr. of compound pancreatin powder 5 oz. of tepid water is added, and then 1 pint of milk at  $38^{\circ}$ . The mixture is maintained at  $38^{\circ}$  for 15 minutes and then boiled to destroy the enzymes. Gruel, arrowroot, etc., may also be pre-digested in the same way. In the place of the water  $\frac{1}{2}$  pint of lime water may be used to the pint of milk. The preparation, if desired for early use, may be kept at  $15^{\circ}$  for 3 or 4 hours, it need not necessarily be boiled.

Peptonised milk is useful in gastric ulcer, intestinal catarrh, for infants' use generally, and in all forms of weakened digestive functions.

**Peptonised Beef Tea** is made by simmering  $\frac{1}{2}$  lb. minced meat with 1 pint of water containing a small quantity of sodium bicarbonate for 2 hours. The cooled mixture is treated with 25 gr. of compound pancreatin powder, set aside in a warm place, boiled and strained.

**Peptonised Beef Jelly and Chicken Jelly** (*Benger's Food, Manchester*). As a restorative, either may be taken alone by teaspoonful or dissolve 2 or 3 teaspoonfuls in a teacupful of boiling water (with pepper and salt). Enriches beef tea, soups, broths, etc. They are readily assimilated by weak digestions. Containing much of the flesh-forming elements of the meat in soluble form these peptonised preparations are superior to non-peptonised extracts.

**Tabellæ Pancreatini** (*B.P.C.*), *syn* PEPTONISING TABLETS, contain pancreatin  $2\frac{1}{2}$  gr. and sodium bicarbonate 10 gr.

### **Trypsinum** (*B.P.C.*).

*Dose.*—3 to 10 grains (0.2 to 0.6 g.)

Trypsin is stated to be produced simultaneously with amyllopsin, and from the same cells in the pancreas. This enzyme is prepared commercially in the form of whitish or yellowish powder, possessing an odour like that of pepsin.

It converts all soluble and many insoluble proteins into amino-acids and polypeptides. Its activity may be determined by the *B.P.* method for trypsin in pancreatin. It is 4 or 5 times as active as pancreatin. The activity is destroyed in general at  $100^{\circ}$ .

**Soluble** slightly in water, more so in glycerin.

It assists digestion in diabetes, and it is occasionally employed for peptonising milk. More usually it is administered as pancreatin.

**Dipankrin** (*Richter, London*). Active principles of pancreas and duodenum. *Dose.*—1 or 2 tablets thrice daily. In pancreatic deficiency.

**Festan** (*Bayer Products, London*). Preparation of pancreatic enzymes consisting of lipase, amylase, protease and hemicellulase in enteric-coated pellets. *Dose.*—1 pellet thrice daily after meals. Dyspepsia due to fermentative insufficiency.

**Liquor Pancreaticus** (*Benger*) (*Benger's Food, Manchester*). *Dose.*—1 to 2 drachms (4 to 8 ml.) in water with meals or in farinaceous gruel, when cool enough to sip to aid intestinal digestion. As an addition to nutritive enemata, a dessertspoonful should be added to beef tea or milk-gruel just before its administration. Will not keep diluted, and presence of acidity or heating over  $140^{\circ}\text{F}$  destroys the ferment.

**Lobulina** (*Napp, London*). Tablets containing extracts of pancreas and yeast for oral administration in diabetes mellitus. *Dose.*—2 to 4 tablets after the principal meals.

**Panacoids** (*Reed & Carmack, Jersey City, Coates & Cooper, London*). Tablets containing desiccated pancreas 2 gr. and desiccated duodenal substance 1 gr. Intestinal indigestion and disorders of the pancreas.

**Pancrepatine** (*Anglo-French Drug Co., London*). Combination of a special extract of the pancreas and hepatic extract in "globules" containing 0.25 g. for the oral treatment of diabetes. [**P1**] **Pancrepatine Compound** contains in

addition 0.05 g of phenazone and 0.002 g sodium methylarsenate in each globule

**Pancrin** (*Richter, London*) Tablets containing pancreas with tannin  
*Dose* —1 or 2 tablets thrice daily Dysfunction of pancreas, dyspepsia, etc

[P1 87] **Panlittol** (*Armour, London*) Tablets containing pancreas  $2\frac{1}{2}$  grains, thyroid B.P.  $\frac{1}{2}$  grain Hypertension

**Pantheric Tablets** (*Parke, Davis, London*) Enteric-coated tablets each containing 5 gr of triple strength pancreatin equivalent to 15 gr of pancreatin B.P. *Dose* —1 to 2 tablets after each meal To assist pancreatic digestion **Pantheric Compound Tablets** contain triple strength pancreatin with sodium glycocholate and sodium taurocholate

**Zymine** (*Fairchild, Bros. & Foster, New York, Burroughs Wellcome, London*) Extract of pancreas containing trypsin, pancreatic diastase and lipase and other enzymes *Dose* —1 to 6 gr twice or thrice daily after food

## PAPAIN

*Dose* —1 to 8 grains (0.06 to 0.5 g)

A proteolytic enzyme occurring as a whitish or light brown amorphous powder, prepared from the juice of the papaw, the unripe fruit of *Carica Papaya* (Passifloraceæ)

**Papaw fruit, fresh**, divested of its seeds, in shape like a vegetable marrow, is a refreshing dessert fruit, with flavour something like the melon. It is commonly used as a table fruit abroad. It is thought to have digestive properties

**Manufacture of Papain.** The fruit, while remaining on the tree, is lightly incised several times at intervals of 2 or 3 days with a bone knife, and juice collected in calabashes containing a little water. The juice is rapidly dried—the coagulated milk being exposed to the sun or artificial heat on glass or linen frames at not exceeding 100°F, subsequently, while still warm, powdered in a drug mill. A dozen fruits yield about  $\frac{1}{2}$  lb of dried granulated crude papain at one tapping

**Uses.** As a digestive in chronic cases of dyspepsia with acid eructations and painful gastric fermentation. It acts in acid, alkaline or neutral media, and like pepsin, has the property of digesting fibrin (as much as 200 times its weight in some cases). Like rennet, it has the property of curdling milk and might be used as a substitute for it. The liquid preparations are suitable for use in cases of enlarged tonsils, after persevering treatment, improvement in nasal breathing can be observed, due to reduction of the swellings. Ulcers and fissures of the tongue have been painted with a solution of papain 1 to 2 in 10 each of glycerin and water

Juice from the unripe fruit is very acid and acts as an efficient vermifuge, and is also a galactagogue and antiscorbutic —S. G. Willmott, *Pharm. J.*, ii/1928, 219

### Elixir Papaini (B.P.C.)

*Dose* — $\frac{1}{2}$  to 1 drachm (2 to 4 ml.).

Contains 3 gr of papain per drachm

**Elixir Papaini** (*Martindale*) *Dose* —1 drachm (4 ml) with meals  
 Papain 8 gr, glycerin 2 dr, hydrochloric acid 2 m, simple elixir to 1 oz.

### Glycerinum Papaini (B.P.C.)

*Dose* — $\frac{1}{2}$  to 1 drachm (2 to 4 ml)

Papain 9% w/v in dilute hydrochloric acid, simple elixir and glycerin.

Is given with meals as a digestive; it has also been used as a pigment for chronic eczema and warts, and has been applied to diphtheritic exudation.

**Liquor Papaini et Iridini (B.P.C.).**

*Dose.*— $\frac{1}{2}$  to 1 drachm (2 to 4 ml.).

Contains 1 gr. of pepsin and 1 gr. of extract of iris per drachm.

[P1-81] **Pilula Papaini Composita.** *Dose*—1 with meals.

Papain 2 gr., extracts of nux vomica  $\frac{1}{2}$  gr., belladonna  $\frac{1}{2}$  gr., aloes  $\frac{1}{2}$  gr. A digestive laxative.

**Ananassa Sativa** (Pine Apple). The juice has been used among the natives in South Africa for diphtheria and diphtheritic sore throat. It has diuretic properties.

The fresh fruit juice contains an active proteolytic enzyme, bromelin, which is destroyed when the juice is heated, or the fruit is canned. Bromelin digests 1000 times its weight of protein in a few hours, and operates equally well in acid, alkaline or neutral medium—S G Willmott, *Pharm J*, ii/1928, 219, *Lancet*, ii/1928, 455.

CARDIAC ŒDEMA in a woman of 30 completely relieved in 3 weeks by daily administration of pineapple juice (juice from a tin of pineapple daily) after digitalis, mercurial compounds, etc., had failed. Urinary output rose in a fortnight from 18 to 20 oz to 60 to 100 oz in 24 hours—B. Macgrath, *Brit med. J.*, ii/1934, 492 Chinese patients suffering from dropsical beri-beri invariably ask for pineapple.—A. J. McClosky, *ibid.*, 572.

## PARAFFINUM

**Paraffinum Durum (B.P.).** *Syn.* PARAFFIN WAX, PARAFFINUM (U.S.P. XI), PARAFFINUM SOLIDUM (P. Dan.). (PARAFFINUM SOLIDUM (P. Helv. V) is ceresin.)

A mixture of several of the harder members of the paraffin series of hydrocarbons from  $C_{21}H_{44}$  to  $C_{30}H_{62}$ ; obtained by distilling shale, separating the liquid oils by refrigeration and purifying the solid product. Colourless, semi-transparent, crystalline, inodorous and tasteless, slightly greasy to the touch. Sp. gr. 0.82 to 0.94. It burns with a bright flame, leaving no residue. Hard paraffins are supplied with various melting-points. B.P. specifies 50° to 60°; U.S.P. XI 50° to 57°.

**Soluble** about 1 in 80 of ether, slightly soluble in dehydrated alcohol, insoluble in water; also insoluble in acetone—a fact of value in the analysis of mixtures.

**Uses.** Principally as an ingredient of ointment bases, especially for protective ointments. Melted paraffin has been employed for the treatment of inflamed joints, sprains, etc. Injections of melted paraffin have been used in plastic surgery.

**Solid Paraffin Injections.** For subcutaneous injection in plastic operations this should be hard paraffin with m.p. 110 to 115°F., not an extempore mixture. Used to improve the size and shape of the nose, ear, etc., where abnormal, also for injecting into cavities after previously swabbing out with antiseptic lotion. The injection should be made in a warm room to allow of the flow of the melted substance through the syringe needle.

**Paraffinoma.** Two cases following paraffin injections. One of the rectum due to liquefied hard paraffin, the other stated to be due to an injection of camphor in liquid paraffin oil in the thigh.—A. T. Bazin, *Brit. med. J.*, ii/1929, 1102.

The publication of various cases of paraffinoma by authors in Europe and America has acted as a warning of the possible dangers of injecting mineral oil into the body tissues. A case of paraffinoma described.—Mason Bolam, *Brit. J. Dermat.*, 1935, 523.

**PAINFUL RHEUMATIC JOINTS.** Envelop the limb (previously shaved) quickly in a thin layer of melted paraffin at a temperature of 80° to 85° and add until layer is 1 to 2 cm. thick. Apply flannel bandage and leave on for 5 hours.—*Per Practitioner*, 1/1928, 397.

Paraffin wax bath over the whole body applied in sections at a time for applying heat to the skin—H. W. Hales, *Lancet*, ii/1931, 586.

### Paraffin Treatment of Burns.

**Paraffin "No. 7"** is made as follows:—Melt hard paraffin 67.75 and add soft paraffin 25 and olive oil 5. Then mix in carefully betanaphthol 0.25 dissolved in eucalyptus oil 2, after the mixture has cooled to about 55°. (The original mentions resorcin 0.25 to 1% as alternative, and that a small quantity of dehydrated alcohol is to be used as solvent.) The finished article melts at about 48°.

**Method of Use.** Wash the burns with sterile water, dry thoroughly, for example with a fan, and spray or apply the melted preparation carefully with a flat camel-hair brush. Cover with a thin layer of wool and a second coating. A preliminary application of 1 to 1000 acriflavine is useful.

**Paraffin "No. 7" Modified** has been made using spermaceti and hard paraffin *p. æq.*, instead of hard paraffin. The preparation melts at 49° and is filled into rubber-capped tubes for use at time of operation, after melting in the water-bath.

**Ambrine** (*Anglo-French Drug Co., London*) A similar preparation advised by B. de Sandfort, containing a compound of paraffin with 5% of oil of amber. Applied in similar manner.

**Granulogen** (*Parke, Davis, London*). Chloretone 22 gr. per oz., and cresylic acid (0.5%) in a basis of paraffin, m.p. 46°. For the treatment of cutaneous lesions. To be melted and applied with a sterile brush or by means of a suitable spray.

**Dental Wax.** Hard paraffin 1 oz., beeswax 6 oz., melt together, add  $\frac{1}{2}$  oz. alkanet and keep warm for 2 hours, then strain and add tincture of tolu 2 dr., otto of rose 5 drops. Generally supplied in sheet  $6\frac{1}{2}$  by  $3\frac{1}{2}$  inches.

**Use.** The sheet is warmed over the flame and moulded carefully over the model. It is used for mechanical purposes prior to vulcanisation.

**Ceresin.** A hard, white paraffin wax, m.p. about 65°, obtained by purifying ozokerite or earth wax, which occurs naturally near petroleum springs, especially in Galicia. Soluble 1 in 170 of ether, 1 in 125 of benzene and 1 in 80 of chloroform. Is used in the manufacture of candles and polishes.

**Paraffinum Liquidum** (*B.P., P. Helv. V, P. Dan.*). *Syn. and Prop. Names.* OLEUM PETROLEI, PETROLATUM LIQUIDUM (*U.S.P. XI*), APEROL (*Cooper, Son & Co., London*), CHRISMOL (*Allen & Hanburys, London*), COLONOL (*Kaylene, London*), INTERNOL (*British Drug Houses, London*), NUJOL (*Stemco, London*),



PAROLEINE (*Burroughs Wellcome, London*), PETROLAINE (*Hewlett, London*), ETC.

*Dose.*— $\frac{1}{4}$  to 1 ounce (7.5 to 30 ml.)

A clear oily liquid obtained from petroleum after the more volatile portions have been removed by distillation. It consists of hydrocarbons ranging from  $C_{16}H_{34}$  to  $C_{21}H_{44}$ . Sp gr 0.880 to 0.895 (B.P.) For spraying, as also for "Toilet Paraffin," is preferred with gravity 0.865 to 0.870, *vide* Paraffinum Liquidum Leve. For internal use a high gravity preferred. Below 0.880 it is not suitable as an internal lubricant. The B.P. Add requires a kinematic viscosity of not less than 64 centistokes at  $37.8^{\circ}$ . U.S.P. XI has two varieties—one termed Heavy, the other Light Liquid Petrolatum—with different viscosities.

A careful clinical comparison of treatment with low (130) viscosity liquid paraffin, sp gr 0.8718 and high (230) of sp gr 0.8902, showed that the latter had a slightly more laxative action and there was decidedly less tendency to leakage. The highly viscous oil was more satisfactory in general.—H. B. Russell and P. C. Brett, *Lancet*, 1/1923, 594

Russian oil contains principally saturated hydrocarbons while American petroleum contains a large proportion of the unsaturated olefines. The Baku oils differ from Pennsylvania and other U.S. oils in consisting largely of hydrocarbons of the naphthene group (saturated single link ring compounds). American oils are best for chlorinating. Cf p 361

**Oleum Petrolei Flavum** and **Huiles Lourdes de Pétrole**. Heavy petroleum oils—products from American petroleum distilling between 280 and 400, sp gr 0.880 to 0.905. Used as a vehicle for hypodermic injections. For the suspension of insoluble mercurial salts, such as calomel, salicylate, succinimide, benzoate and yellow oxide of mercury, 1, 5 or 10% mixtures being employed.

**Vaseline Liquidum**. *Syn.* HUILE DE VASELINE, "VASELINE LIQUID" (*Fr. Cx*), is prepared from Caucasian petroleum by purifying the fractions between  $335^{\circ}$  and  $440^{\circ}$ . Sp gr about 0.875, *i.e.*, it approximates Paraffinum Liquidum in character. Employed in Huile Grise *q.v.* FF VIII, P Ital V and P Belg. IV are similar.

**Uses.** Liquid and soft paraffin are employed as electuaries or lubricants in constipation. Also of use internally for colitis in children. By its lubricating action, taken regularly, it may avert appendicitis. It is a good catheter lubricant.

It is used as a basis for laryngeal and nasal spray solutions or pigments, but for these purposes the B.P. oil is too viscous, and Paraffinum Liquidum Leve (*vide infra*) is preferable. Alkaloidal bases are, in general, only slightly soluble in liquid paraffin. A little oleic acid added assists solution.

Its action on the bowel is due in great measure to its ability to form emulsions, holding about 15% more water than usual in the stool.—*Per Pharm J*, 11/1927, 461.

Liquid paraffin should be given  $\frac{1}{4}$  hour before food. 7 to 10 m. of Tinct. Belladonnæ after breakfast and dinner helps the onward passage of contents of unhealthy colons.—A. Grehm-Stewart, *Lancet*, 11/1930, 874

No "a priori" reason why paraffin should replace other laxatives. May be irritant. The primary defect in constipation is in the neuro-muscular mechanism controlling peristalsis in the stomach and small intestine, and mass movements in the colon—these movements are not necessarily stimulated by either bulky or rough residue.—L. J. Green, *Lancet*, 11/1930, 993, 1044.

Paraffin is capable of inhibiting the action of the proteolytic ferments, but this action is modified when the oil is emulsified. Patients who complain of "seepage" of oil from the rectum whilst taking a small or moderate dose are incapable of providing the natural emulsifying agents, and this defect is also

probably responsible for the loss of weight and digestive disturbances occasionally observed in those taking liquid paraffin—F B Parsons, *Practitioner*, 11/1932, 74

**ECZEMA ANI** consequent on the taking of liquid paraffin for chronic constipation—R Gibson, *Brit med J*, 1/1927, 876

**HÆRSES ZOSTER** Paraffin dressings found of great value for the relief of pain, effective only during the eruptive period—Howard Fox, *per Prescriber*, Feb., 1923, 83.

**Creosoted Oil.** (Calot's formula) Liquid paraffin 70 g., sterilised by heating for  $\frac{1}{2}$  hour. Allow to cool and add in order creosote 5 g., guaiacol 1 g., iodoform (sterile) 10 g., ether 30 g.

Used as a wound dressing

**Injection of 10 ml weekly of Calot's fluid with olive oil in place of liquid paraffin** of distinct value following aspiration of cold abscesses and in treatment of white swellings of joints **Calot's No. 2 Paste**—Phenol camphor 3 g., naphthol camphor 3 g., guaiacol 8 g., iodoform 10 g., lanolin 150 g., spermaceti 100 g., of value for injection in sinus formation in disease of hip, spine and knee 10 ml injected into sinus at temperature of 103°, repeated every fourth day for 10 occasions. Contraindicated in albuminuria and septic infections causing pyrexia—R Pollock, *Lancet*, 1/1927, 225

**OTORRHEA** Calot's solution of value. Instil 5 to 10 drops into ear canal. To get fluid into Eustachian tube close opening of external canal by pressing tragus against canal wall and bringing alternate pressure to bear on it so as to cause pumping action on mixture, and continue until patient feels medicament in throat. Repeat nightly for a week. When secretion becomes thin discontinue and dry up with insufflations of boric acid powder—I Hamick, *J Amer med Ass*, 11/1929, 66. Success in 85% of cases—J C Scal, *Med J Rec*, 1933, 244

### **Emulsio Paraffini Liquidi Alkalina (B P C)**

**Dose**—1 to 4 drachms (4 to 16 ml)

Mixture of magnesium hydroxide 1 part and emulsion of liquid paraffin with agar 3 parts

### **Emulsio Paraffini Liquidi Composita (B P C)**

*Syn* EMULSIO PARAFFINI CUM AGAR ET PHENOLPHTHALEINO

**Dose**—As above

The formula is as above, incorporating also phenolphthalein  $1\frac{1}{2}$  gr per ounce

### **Emulsio Paraffini Liquidi cum Agar (B P C)**

**Dose**—1 to 4 drachms (4 to 16 ml), or more if requisite, morning and evening. Children 1 to 2 drachms. Contains 50% v/v of liquid paraffin and 0.75% w/v of agar

**Emulsum Petrolati Liquidi (U S P XI)** *Average dose*—1 ounce (30 ml). Liquid petrolatum 50% with acacia or agar, etc., syrup and alcohol, and 0.004% of vanillin

**Emuls. Petrol. c. Agar (N I F)** Agar 36 gr., liquid paraffin 4 oz., acacia 87½ gr., tragacanth 14 gr., vanillin 1½ gr., elixir of saccharin 8 m., benzoic acid 7 gr., double chloroform water to 8 oz

**Emuls. Petrol. c. Phenolphthalein. et Agar (N I F)** Agar 36 gr., liquid paraffin 4 oz., phenolphthalein 16 gr., glycerin 390 m., acacia 60 gr., tragacanth 20 gr., glycerin of boric acid 112 m., sodium benzoate 18 gr., vanillin 1½ gr., double chloroform water to 8 oz

### **Emulsio Paraffini Liquidi cum Hypophosphitibus (B.P.C)** *Syn* EMULSIO PETROLEI CUM HYPOPHOSPHITIBUS

**Dose**—1 to 4 drachms (4 to 16 ml.).

Liquid paraffin 50% v/v with 1-gr. each of sodium and calcium hypophosphites per drachm.

**Emulsio Paraffini cum Pancreatino.** *Dose*—2 to 4 drachms (8 to 16 ml.) The same as the preceding emulsion with the addition of 10% v/v of solution

of pancreatin in place of an equal volume of water. For the intestinal stasis of tuberculous children, drachm doses of this preparation promote healthy function of the bowel.

**Emulsio Paraffini et Bismuthi.** *Dose.*—1 ounce (30 ml.) first thing in the morning and at bedtime, followed by  $\frac{1}{2}$  tumblerful of moderately hot water.

Liquid paraffin 1 oz., clove oil 10 m., sodium bicarbonate and compound tragacanth powder, of each 1 dr. Emulsify with chloroform water  $\frac{1}{2}$  oz. and solution of bismuth and ammonium citrate 1 dr., and add in portions chloroform water to 8 oz.

The small dose of bismuth is intentional. In some cases larger quantities may prove constipating. The formula is varied to suit the case, e.g., peppermint oil 10 m. may replace the clove oil, varying doses of bismuth salicylate or subgallate may replace the bismuth solution, and where there is constipation, Vinum Aloes or compound tincture of aloes  $\frac{1}{2}$  to 1  $\frac{1}{2}$  oz. may be incorporated.

Catarrh of the alimentary tract is frequently responsible for toxæmia due to insufficient or impeded action of the liver and pancreas. This condition is often the cause of affections of the circulatory system (heart troubles, etc.), coupled with evidence of rheumatoid arthritis and of fibrositis.

**Emulsio Paraffini cum Rhamno Frangula.** *Dose.*— $\frac{1}{2}$  to 1 ounce (15 to 30 ml.) Liquid extract of buckthorn bark 1 oz., liquid paraffin 4 oz., benzoic acid 5 gr., Irish moss decoction to 8 oz. A mild laxative.

### **Mistura Magnesii Hydroxidi et Paraffini Liquidi (B.P.C.)**

*Dose.*—1 to 4 drachms (4 to 16 ml.).

Liquid paraffin 30% v/v emulsified in mixture of magnesium hydroxide by means of acacia, or by using an homogenising machine, in which case no acacia is needed.

### **Parogenum (B.P.C.).** *Syn.* VASOLIMENT, LIQUID PAROGEN.

Liquid paraffin 40% v/v with oleic acid, ammoniated alcohol and alcohol 90%.

**Agarol Brand Compound** (Warner, London). An emulsion of liquid paraffin with agar. For formula, see Vol. II.

**Colactin** (Spicer, Watford). Paraffin emulsion containing 40% of lactose. No. 1, plain; No. 2, with phenolphthalein.

**Cristolax** (Wander, London). A compound of 50% of liquid paraffin with 50% of malt extract in powder form.

**Fructolax** (Savory & Moore, London) *Dose.*—2 to 3 drachms at bedtime. A laxative containing about 80% soft hydrocarbon with fruit basis.

**Maltaffin** (Martindale, London). *Dose.*—1 to 2 teaspoonfuls at bedtime. Children,  $\frac{1}{2}$  to 1 teaspoonful, increased if necessary. A combination of liquid hydrocarbon oil with malt extract as an electuary. Suitable for children. The oily taste is largely masked.

**Obstisan** (Chemische Fabrik Gustrow, Gustrow & Meckl.; Braun, London). Emulsion of liquid paraffin with invert sugar.

**Olgar** (Parke, Davis, London). Emulsion of refined liquid paraffin and agar.

**Paraffagar** (Martindale, London). A combination of hydrocarbon oil with agar in the form of a jelly as an efficient electuary, without weakening effects.

*Dose.*—1 to 2 drachms at bedtime. Children,  $\frac{1}{2}$  to 1 drachm, increased if necessary.

**Paraffagar with Phenolphthalein.** *Dose.*—1 to 2 drachms, containing phenolphthalein  $\frac{1}{2}$  gr. in 1 dr.

**Petrolagar** (Petrolagar Laboratories, London). An emulsion of liquid paraffin 65%, with agar. Also available with phenolphthalein 1  $\frac{1}{2}$  gr. per oz., or alkaline (with magnesium hydroxide).

**Semprolin Emulsion** (Semprolin Co., London). An emulsion containing 60% liquid paraffin. Combinations with bismuth and pepsin, glycerophosphates, hypophosphites, iron, lecithin, guaiacol, malt, salol, etc., are made. Semprolin Cream containing 90% liquid paraffin and Semprolin Carminative are also prepared.

**Paraffinum Liquidum Leve (B.P.C.).** *Syn. and Prop. Name.* SPRAY PARAFFIN, PARAFFINUM LIQUIDUM PRO NEBULIS, PAROLEINE (for spraying) (*Burroughs Wellcome, London*).

A variety of liquid paraffin of lower gravity and lower viscosity than the oil for internal administration, and more suitable for the preparation of sprays.

**Paraffinum Molle (B.P.).** *Syn. and Prop Name* PETROLATUM (*U.S.P. XI*) and PETROLATUM ALBUM (*U.S.P. XI*), PETROLEUM JELLY, VASELINA (*F.E. VIII*), VASELINUM (*P. Ital. V, P. Belg IV, P. Helv. V, P. Dan.*), VASELINE (*Cheesebrough Manufacturing Co., London*).

A white (Paraffinum Molle Album) or yellow (Paraffinum Molle Flavum) semi-solid mixture containing some of the softer or more fluid members of the paraffin series of hydrocarbons from  $C_{15}H_{32}$  to  $C_{20}H_{42}$ . M.p. of the white variety  $40^{\circ}$  to  $46^{\circ}$ , of the yellow variety  $38^{\circ}$  to  $46^{\circ}$  (*U.S.P. XI* requires  $38^{\circ}$  to  $54^{\circ}$ ). Is usually obtained by purifying the less volatile portions of petroleum.

**Soluble** in alcohol slightly, freely in ether and chloroform, insoluble in water and in acetone. When melted, it mixes with oil, and many waxes, oleates and oleic acid.

Soft paraffin is not readily absorbed, but is emollient, protective and useful as an ointment base for surface action.

**Glegg's Mixture** consists of 3 parts liquid paraffin and 1 part of white soft paraffin, flavoured with rosettol (or with  $\frac{1}{2}$  gr. of menthol per oz.). Applied twice daily by a nasal pipette to the back of the nose for the prevention and treatment of the common cold —E. P. Poulton, *Lancet*, 1/1932, 933. If the cold cannot be aborted entirely by this treatment, at least it develops into a relatively mild affair —E. P. Poulton and F. A. Knott, *Practitioner*, 1/1936, 28.

**Confectio Paraffini (L.H.)** Dose —1 to 2 drachms (4 to 8 g.)

Yellow soft paraffin 16 oz., alkanet root 42 gr., oil of lemon 32 m., oil of bitter orange 32 m.

**Lotio Paraffini Composita.** Soft paraffin 3 oz., balsam of Peru 2 dr., mercuric oleate 60 gr., olive oil  $1\frac{1}{2}$  oz. To be applied with a stiff brush. For parasitic skin diseases.

**Oculentum Simplex (B.P.C.).** A sterile mixture of wool fat and yellow soft paraffin used as a basis for eye ointments of the B.P. and B.P.C.

**Paranol (B.P.C.).** An emulsion of water in wool fat and soft paraffin.

**Unguentum Paraffini (B.P.).**

White beeswax 2, hard paraffin 8, yellow or white soft paraffin 90.

Unguentum Paraffini made with hard paraffin (m.p.  $54^{\circ}$  to  $57^{\circ}$ ) 27, soft paraffin 70, beeswax 3, is suitable for use with the atmospheric temperature  $15^{\circ}$ . May be modified to meet the exigencies of climate and temperature.

The addition of 3% of beeswax makes the ointment more uniform.

A hard paraffin with somewhat low melting point, e.g.,  $46^{\circ}$  to  $52^{\circ}$ , is best. Melt together and set aside to crystallise (or allow to cool on the water bath) and then mill, rub down, or sieve again.

A small quantity of wool fat added to soft or liquid paraffins enables the production of a stable emulsion, *vide* Paranol.

**Unguentum Simplex (B.P.).**

Wool fat 5, hard paraffin 10, yellow or white soft paraffin 85.

**Unguentum (U.S.P. XI)** *Syn* SIMPLE OINTMENT Wool fat 5, white wax 5, white petrolatum 90.

**Petroleum Benzine** is the fraction distilling below 150°, sp. gr below 0.750. This is used for cleaning purposes *Benzine means petroleum benzine*. Distinguish from benzene (benzol), the product obtained from coal tar, *q.v.* On fractionation it yields various products such as mineral naphtha or benzolin (boiling range 70° to 95°), ligroin or petroleum naphtha (boiling range 90 to 120°), and petrol.

**Petroleum Leve (B.P.C., P. Dan., P. Helv. V)** *Syn* PETROLEUM SPIRIT, PETROLEUM ETHER  $C_6H_{12}$  = 72.1 principally. At least 95% distils between 60° and 70°, and has sp. gr. of 0.620 to 0.700. *P. Helv. V* requires 90% to distil below 60°, sp. gr. 0.65 to 0.67.

**Benzinum Purificatum (U.S.P. XI)**, *syn* PETROLEUM ETHER, is purified petroleum benzine. It has sp. gr. 0.634 to 0.660, and distils entirely between 35° and 80°. **Petroleinum (P. Belg. IV, P. Jap. IV)** has sp. gr. 0.64 to 0.67, boiling-range 50° to 75°. **Pétrole léger (Fr. Cx.)** has sp. gr. about 0.6 and distils entirely below 50°. Higher fractions of petroleum are white spirit or turpentine substitute (boiling range 140° to 220°), illuminating or solar oils (various boiling-ranges up to 300°) and heavy lubricating oils.

**Kerosene.** Distilled from petroleum and has a boiling range of 150° to 300° with sp. gr. about 0.800 to 0.811. Is used as an illuminating and fuel oil.

Kerosene poisoning in children—4 cases with 1 death—J. P. Price, *J. Amer. med. Ass.*, 11/1932, 214.

**Lefroy's Crude Mineral Oil Emulsion.** *Syn.* PETROLEUM INSECTICIDE.

Crude mineral oil (kerosene) 110, soft soap 50 (whale oil soap is specified) with about 10 of water to form a jelly. For use against lice, fleas, flies, etc., both destroying them, preventing their further attack and thereby acting as a prophylactic to many forms of infectious disease. It is used like ordinary soap for washing. If a little be allowed to dry into the clothes vermin will not approach. The same effect is secured by rubbing a little over the skin—H. Maxwell-Lefroy, *Lancet*, 1/1915, 1150.

Favus has been cured by soaking with petroleum of commerce.

**Huile de Pétrole (Fr. Cx.)** has sp. gr. 0.800, distilling between 130° and 260°, from American petroleum. Flash point not below 35°.

**"Petrol."** *Syn.* GASOLINE, "MOTOR SPIRIT." Sp. gr. 0.720 to 0.750. Data as to b.p. and commercial varieties—Vol. II.

**Antidotes.** Empty stomach by emetic or stomach tube. Keep patient warm but in fresh air. Give stimulants. Artificial respiration if necessary.

Epidemic of diphtheria or scarlet fever in an institution may be avoided by swabbing the children's throats with petrol as soon as throat trouble is suspected. It can be used as a spray, a method not objected to by children. Its taste is not unpleasant and it causes no burning or disagreeable sensation in the throat—G. A. Stephens, *Prescriber*, 1935, 366.

**Tetra-Ethyl Lead.**

A very active and dangerous poison, far more so than any inorganic lead compound—only a few mg. a day will cause cumulative poisoning. In the works of the Standard Oil Co., New Jersey, 5 employees died and 30 others were affected. For treatment large quantities of alkalis recommended—*Brit. med. J.*, 1/1928, 61, 64, 75. Further investigation necessary, *ibid.*, 363, 366.

In a family car using 107 gals. of ethyl petrol (3.5 g. of lead per gal.) 75% of the lead went into the air and the rest into the car parts—*Daily Mail*, Apr. 13, 1928.

Ethyl petrol acquitted—*Lancet*, 1/1930, 820. Report of proceedings of Committee of Enquiry.—*Brit. med. J.*, 1/1928, 770, 871, 1033, 1073.

Tetramethyl lead of comparatively low toxicity compared with other lead compounds. M.L.D. of a number of organic lead compounds given.—J. S. Buck and D. M. Kumro, *J. Pharmacol.*, 1930, 171.

**Cera Alba (B.P., U.S.P. XI, P. Helv. V, P. Dan.)** is obtained by bleaching yellow wax (**Cera Flava B.P., U.S.P. XI, P. Helv.**

*V. P. Dan.*), the secretion formed by *Apis mellifica* (Order, Hymenoptera) and used by the insect to form the cells of the honeycomb. Soluble in warm ether, in chloroform and in fixed and volatile oils; sparingly soluble in cold alcohol 90%. M p 62° to 64°.

**Ceratum** (*U.S.P. XI*) White wax 3, benzoated lard 7

**Cera Aseptica** (*B.P.C.*) A sterile mixture of white beeswax and almond oil containing 1% of salicylic acid

**Horsley's Wax.** An aseptic wax for surgeons' use Yellow beeswax 7, phenol 1, olive oil 2 It is employed warm at a temperature such that its consistence is just sufficiently soft for easy manipulation It is heated at temperature of boiling water 5 minutes and then poured into saline or mercuric chloride solution at 105°F, from which it is used during the operation—P Sargent, *Brit med J*, 11/1922, 1200

As a plugging for the exposed cancellous bone in drainage for empyema in tuberculous children—free drainage effected—Dennis Browne, *Lancet*, 11/1930, 736

**Oxyrocroceum Plaster** (*P. Helv. V*) Yellow beeswax 35, colophony 25, elemi 10, ammoniacum 5, galbanum 5, myrrh 5, Venice turpentine 12, saffron 1, extract of rhatany 2

**Carnauba Wax** is a hard yellowish or greenish wax exuded from the leaves of *Copernicia cerifera* (Palmæ), m p about 85°, sp gr about 0.995 Is used in polishes

**Japan Wax** is obtained from the berries of various species of *Rhus* It is a pale yellowish wax, becoming white externally on keeping M p about 55°, sp gr about 0.995 Is used in polishes

**Cetaceum** (*B.P.C.*, *U.S.P. XI*, *P. Helv. V*, *P. Dan.*) *Syn* BLANC DE BALEINE (*Fr. Cx.*).

*Dose.*—8 to 30 grains (0.5 to 2 g.)

Spermaceti is a white, unctuous crystalline substance (m p 42° to 50°), obtained from *Physeter macrocephalus* and other species of whale, e.g., *Hyperoodon rostratus* Consists chiefly of cetyl palmitate,  $C_{15}H_{31}COOC_{16}H_{33}$  - 480.5 Soluble 1 in 1½ of chloroform and about 1 in 7 of ether, also in hot alcohol A common ingredient of cold creams. A good addition to theobroma suppositories for hot climates An emulsion (with acacia or egg yolk, using spermaceti powdered with a little alcohol) has been administered as a demulcent for coughs

**Oleum Cetacei** is obtained by removing the spermaceti which separates from the crude oil on standing It is a thin yellow oil used for burning and as a lubricant

**Unguentum Cetacei** (*B.P.C.*) contains 20% of spermaceti in white beeswax and liquid paraffin

**Alcohol Cetylicus** (*P. Helv. V*) *Prop Name* LANETIL WAX (*Ronschelm & Moore, London*).  $CH_3(CH_2)_{14}CH_2OH$  - 242.27

In white crystalline masses, greasy to the touch, m p 48° to 50° Soluble in ether, chloroform, carbon disulphide and boiling alcohol

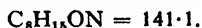
**Unguentum Cetylicus** (*P. Helv. V*) Cetyl alcohol 4, wool fat 10, white soft paraffin 86

## PASTILLI

Pastilles consist of a basis of gelatin with varying quantities of glycerin. The medicament is dissolved or suspended in the melted mass, which is then moulded in oil-lubricated moulds.

The *B.P.C.* recommends **Glycogelatin** as a basis for pastilles. This has gelatin 20, glycerin 40, sucrose 5, citric acid 2, sodium benzoate 0·2, oil of lemon 0·1, solution of bordeaux B 1, triple orange-flower water 6·25. The gelatin is softened in water, the glycerin added and the mass evaporated down to 85. The other ingredients are then incorporated. This basis gives a soft pastille which quickly dissolves in the mouth. As the medicament is intended to have a prolonged local action, the basis should be firm enough to ensure that the pastilles dissolve very slowly. The usual commercial medicated pastille contains a higher proportion of gelatin and dissolves slowly in the mouth. They are moulded in dry starch moulds and then thoroughly dried in trays for several weeks.

## PELLETIERINA



[P1] "*Alkaloids, the following; their salts, simple or complex:—Pomegranate, alkaloids of.*"

[81] "*Alkaloids, the following; their salts, simple or complex.—Pomegranate, alkaloids of, except substances containing less than 0·5% of the alkaloids of pomegranate.*"

[83] "*Alkaloids:—Pomegranate, alkaloids of—in pomegranate bark.*"

[86] "*Alkaloids:—Pomegranate, alkaloids of—specify proportion as the proportion of any one alkaloid of pomegranate that the preparation would be calculated to contain on the assumption that all the alkaloids of pomegranate in the preparation were that alkaloid.*"

*Dose.*—2 to 6 grains (0·12 to 0·4 g.).

A mixture of alkaloids obtained from pomegranate stem and root bark, *Punica Granatum* (Punicaceæ), in minute shining white crystals. The alkaloids are at least four in number; their amount varies between 0·5 and 0·7%. In addition the bark contains 20% of tannin.

[P1-81] **Pelletierine**, *syn.* PUNICINE, *dose*—2 to 8 grains, is  $\beta$ -2-piperidyl propaldehyde, or in other words the aldehyde of conine. It is a colourless volatile liquid becoming brown on exposure. Soluble 1 in 23 of water, miscible with organic solvents.

[P1-81] **Pelletierinæ Sulphas**. *Syn.* PUNICINE SULPHATE, PELLETIERINUM SULFURICUM (*Fr. Cx.*).  $(\text{C}_8\text{H}_{15}\text{NO})_2\text{H}_2\text{SO}_4 = 380\cdot3$ .

*Dose.*—2 to 8 grains (0·12 to 0·5 g.).

Consists mainly of the sulphates of pelletierine and *iso*-pelletierine. Colourless crystals becoming yellow on keeping. As a remedy for tape-worm: 5 to 8 grains taken fasting, followed by a full dose of compound tincture of jalap; for children of 13 years, half the above dose, and for infants one-tenth.

*Fr. Cx.* provides complete method of manufacture from the pomegranate root bark. The dose is usually 0.3 g. with 0.4 g. of tannin and 2.5 g. of syrup. Max. single dose is 0.4 g.

[P1 81] **Pelletierinæ Tannas** (*B.P.*, *U.S.P. XI*).

*Dose.*—2 to 8 grains (0.12 to 0.5 g.). *U.S.P. XI* average dose 4 grains.

A mixture of the tannates of the alkaloids. A light yellow powder. Soluble about 1 in 700 of water, and about 1 in 80 of alcohol 90%; insoluble in chloroform. As a tæniacuge, 8 grains followed in 2 hours by an ounce of castor oil proved an effectual dose, causing neither colic nor headache.

**Granati Fructus Cortex** (*B.P.C.*). *Syn.* POMEGRANATE RIND.

*Dose* — $\frac{1}{4}$  to  $\frac{1}{2}$  drachm (1 to 2 g.)

The dried pericarp of the fruit of *Punica Granatum* (*Punicaceæ*). Used as a decoction in diarrhoea and as a douche in leucorrhœa. Contains about 28% of gallotannic acid

**Granati Radicis Cortex** (*B.P.C.*, *P. Helv. V*, *P. Dan.*). *Syn.* GRANATI CORTEX, GRANATUM, POMEGRANATE, MELOGRANO (*P. Helv. V*).

*Dose* — $\frac{1}{4}$  to  $\frac{1}{2}$  drachm (1 to 2 g.)

The dried bark of the stem and root, containing about 0.5 to 0.9% of alkaloids, chiefly pelletierine and pseudo-pelletierine. Used to expel tapeworm, the 1 in 5 decoction being given in doses of 2 ounces every two hours for four doses, the treatment being preceded and followed by the administration of a purge.

Better results in tapeworm by passing into duodenum by Einhorn's catheter 150 g. of powdered root bark infused for 12 hours in a litre of water, and boiled down to one half. Before use, warm to 100°F and give three doses of 65 ml. at half-hour intervals, followed by laxative, after which catheter is withdrawn. Only two failures in 19 cases — *Lancet*, ii/1926, 1354

**Spigelia.** *Syn.* INDIAN PINK, PINK ROOT. *Dose* — $\frac{1}{4}$  to 1 drachm (2 to 4 g.). The dried rhizome and rootlets or the dried entire plant, *Spigelia marilandica* (*Loganiaceæ*). Anthelmintic for round-worms, being administered in conjunction with a purge either as powder or as an infusion. Should be followed by a saline purge.

## PEPSINUM

*B.P.*, *U.S.P. XI*, *P. Helv. V*.

*Dose.*—5 to 10 grains (0.3 to 0.6 g.) either with or immediately before or after meals, in a pill or cachet. It is not unpalatable sprinkled on meat like pepper. *U.S.P. XI* average dose 8 grains.

A proteolytic enzyme obtained from the gastric mucous membrane of the pig, sheep or calf, Pepsina Porci being usually preferred. Occurs as a light, yellowish-brown powder or in translucent scales or granules. It is supplied to dissolve 2500 (*B.P.*), 3000 or 5000 times its weight of freshly coagulated egg albumen. *U.S.P. XI* requires it to digest 3000-3500 times its weight of egg albumen.

The gastric juice of man is believed to contain several distinct digestive ferments, the chief being:—

- (a) Pepsin.—This changes protein (fibrin, albumen, etc.) into peptones in an acid medium, 0.2% of hydrochloric acid being the most advantageous. To this the medicinal pepsins owe their activity.
- (b) Curdling ferment, which curdles the casein of milk; this is very active in the stomach of the calf, and can be dried.



**Incompatibility** depends to a great extent on concentration of the diluent fluid. A small quantity of electrolyte seems essential to enzyme action. Salts present in quantity hinder the enzyme. The following if present in strong proportion prevent action:—

Alcohol,	Copper Sulphate,	Potassium Salts (Chloride,
Alkalis,	Extract of Malt,	Bromide, Iodide),
Alum,	Magnesium Sulphate,	Sodium Chloride,
	Paraldehyde,	Hexamine

Asbestos, as also aluminium hydroxide, has the power of removing pepsin and other ferments from solutions

#### **Soluble and Insoluble Pepsins (Commercial).**

**Insoluble Pepsins** are of two kinds, one precipitated by salt, and one made directly from the selected membranes without digestion, but purified by washing in spirit. These require a small quantity of hydrochloric acid to effect solution in water.

**Soluble Pepsin** is made by self-digestion of the membranes and subsequent dialysis of the resulting peptone, thus leaving the peptic power in a soluble and more isolated form. It is then dried on glass plates, being sold in scale or powder form.

**Uses.** As a digestive, small doses, either in form of powder, or cachets, or one of the following preparations with or after meals, are useful. The *Tabelle*, masticated, are specially convenient. In sprue and hill diarrhoea, pepsin has given good results. In the vomiting of pregnancy, pepsin in dose of 7 to 8 grains has been advocated as of service.

Pepsin and hydrochloric acid given immediately after eating may inhibit carbohydrate digestion in the stomach. It should not be taken until from 30 to 45 minutes after eating — Prof. Diner, per *Prescriber*, Feb., 1920.

**GASTRIC AND DUODENAL ULCERS** (600 cases) cured by subcutaneous injections of a 1% pepsin solution (freed from albumin by pressure filtering through clay and containing phenol). Begin with 0.2 ml thrice daily or every other day, increasing by 0.1 ml to 0.5 ml, repeating this for 12 injections, and then decreasing in the same way to 0.2 ml. Injections said to be harmless and painless. Give olive oil before meals and bismuth after meals. Avoid belladonna and sodium bicarbonate, and give mixed diet — K. Glaessner (Vienna), *Lancet*, 1/1932, 78.

**Achlorhydria** in a variety of conditions cured by pepsin and hydrochloric acid — T. H. Oliver and J. F. Wilkinson, *Brit. med. J.*, ii/1930, 1048.

#### **Elixir Pepsini (B.P.C.)**

*Dose.*— $\frac{1}{2}$  to 1 drachm (2 to 4 ml.)

Contains about 3 gr. of pepsin per drachm.

#### **Glycerinum Pepsini (B.P.C.).**

*Dose.*—1 to 2 drachms (4 to 8 ml.) in water.

A solution of pepsin 10% w/v in acidified glycerin and water. This is a very active solution. If made with good scale pepsin it keeps indefinitely.

#### **Glycerinum Pepsini Fortius (B.P.C.).** *Syn* GLYCEROL OF PEPSIN.

*Dose.*— $\frac{1}{2}$  to 1 drachm (2 to 4 ml.)

Contains about 8 gr. of pepsin per drachm, in acidified glycerin, simple elixir and water.

#### **Liquor Pepticus (B.P.C.)**

*Dose.*—1 to 2 drachms (4 to 8 ml.).

Contains 1 in 8 of stronger glycerin of pepsin in acidified diluted alcohol.

**Liquor Pepticus (Benger's)** (*Benger's Food Ltd., Manchester*)

*Dose* —1 to 2 drachms (4 to 8 ml) in a wineglassful of water with meals. An active solution of the ferments in weak alcohol.

**Liquor Pepsini et Caffeinae** (*Martindale*).

*Dose* —2 to 4 drachms in water after meals. Glycerin of pepsin 60 m, caffeine citrate 2 gr, water to 2 dr. As a digestive and restorative. The presence of caffeine is stated to increase the activity of pepsin.

**Pulvis Pepsini Compositus (B.P.C.)**

*Dose* —10 to 30 grains (0.6 to 2 g).

Pepsin 15%, pancreatin 10%, diastase 1%, with lactic and hydrochloric acids and lactose.

**Pepana** (*Burroughs Wellcome, London*). "Tablets" contain pepsin, pancreatin and calcium lactophosphate, of each 1 gr. The external sugar-coating dissolves in the stomach, exposing the pepsin, whilst the pancreatin enclosed in a keratin coating dissolves in the intestine.

**Tabellæ Pepsini.** *Dose* —1 or 2 with or after meals.

These have 3 grains of pepsin in each in combination with chocolate.

**Tabellæ Pepsini et Bismuthi,** *dose* —1 or 2 just before or with meals, contain 3 grains of bismuth subnitrate added to the above.

**Tabellæ Pepsini et Caffeinae.**

Contain 3 gr. of pepsin with 2 gr. of caffeine. *Dose* —1 to 2 after a meal. Digestive and tonic.

**Vinum Pepsini (B.P.C.)** *Dose* —1 to 2 drachms (4 to 8 ml) with meals.

Contains pepsin 2 gr. per drachm, hydrochloric acid 1 in 80 and glycerin in sherry-type wine.

**Peptenzyme** (*Reed & Carnrick, Jersey City, Coates & Cooper, London*)

*Dose* —10 to 20 grains (0.6 to 1.2 g) before or after meals and at bedtime.

A preparation containing the enzymes which enter into the process of digestion suitable for varied types of indigestion. Also supplied in tablets, granules and elixir.

**Seriparium (B.P.C.)** *Syn.* RINNET, RENNIN

The partially purified, milk-curdling enzyme from the glandular layer of the fourth or true digesting stomach of the calf, occurring as greyish- or yellowish-white scales or powder slowly soluble in water. It deteriorates when stored. Coagulates not less than 25,000 times its weight of fresh cows' milk.

## PEPTONUM

*B.P.C.*

*Dose* —5 to 15 grains (0.3 to 1 g);  $\frac{1}{8}$  to  $1\frac{1}{2}$  grains (0.01 to 0.1 g.) by injection.

A mixture of cleavage products of proteins consisting of proteoses with peptones and amino-acids.

Prepared from meat (the proteins and albuminoids), peptonised either by acidulation and heat under pressure, or by artificial digestion with pepsin or trypsin, and freed from saline matter. Meat products may be treated by allowing to stand at room temperature for 5 or 6 days with 5 times their bulk of 70% sulphuric acid. Water is added, the mixture cooled and neutralised with barium hydroxide, and the peptone solution dried *in vacuo*. Phosphoric acid may also be employed. Alternatively

casein or gelatin are operated upon in alkaline solution, the last-mentioned by aid of pancreatin.

**To test a peptone as to suitability for clinical use.**

(a) Add an equal volume of saturated aqueous ammonium sulphate solution to a 10% solution of the peptone and stir with a glass rod. If satisfactory, a sticky precipitate, which adheres to the rod, comes down.

The sample should also respond to half-saturated ammonium sulphate—this precipitates the primary proteoses.

(b) Add to a few ml. of a solution, in a test tube, two or three drops of strong nitric acid. A copious white precipitate is immediately produced, consisting of primary proteoses. On heating, the precipitate entirely dissolves, and re-appears on cooling.

**Injectio Peptoni (B.P.C.).**

**Dose.**—3 minims (0.2 ml.) gradually increased to 25 minims (1.5 ml.) by intravenous or intramuscular injection.

A sterile neutral solution containing 5% *w/v* (for intravenous use), or 7.5% *w/v* (for intramuscular use) of peptone.

Peptone injections are employed for non-specific desensitisation in allergic conditions, particularly in asthma, hay fever, angioneurotic oedema, cyclic vomiting and the migraine-epilepsy syndrome.

**Non-Specific Protein Therapy**

Non-specific protein therapy is the treatment of disease by the injection of proteins, either bacterial or non-bacterial, which, by provoking a defensive reaction (rise of temperature, leucocytosis, etc.) similar to that produced by the invasion of the organism by a specific foreign protein, enables the patient to desensitise or immunise himself. The actual mechanism of this reaction is still obscure, though according to A. J. Clark (*Brit. med. J.*, 1/1923, 315) the active agent is a product of protein decomposition. The washing of tissue fluids into the circulation produces changes in the blood such as leucopenia followed by leucocytosis; increase in young and atypical erythrocytes and platelets; increase in fibrinogen, globulin, thrombokinas and blood sugar, in the non-protein nitrogen content, and in the proteolytic ferments; and finally an increase in the permeability of the cell membranes and capillaries.

Numerous substances have been employed to produce this protein shock. Amongst the more important of these are (1) peptones and proteoses; (2) milk and preparations made from milk; (3) vaccines (used non-specifically) and tuberculins; (4) artificially induced diseases, such as malaria; (5) blood and sera; (6) vegetable and animal proteins, such as pollen extracts. These are dealt with in this order in the following pages.

**(1) Peptone.**

The treatment of bronchial asthma by immunisation with small graded doses of peptone has been employed with success. The method was introduced in 1917 by A. G. Auld.—*Brit. med. J.*, 1/1917, 580; ii/1918, 49, 1/1920, 567; 1/1921, 696; i/1922, 835; i/1925, 448, 762; ii/1926, 732; 1/1927, 829; *Lancet*, 1/1923, 790.

**CASES RESISTING TREATMENT:—**

Many of those with chronic bronchitis and developed emphysema, and cases presenting any degree of cyanosis, even without bronchitis; also those in whom, apart from asthmatical paroxysms, a more or less oppressed condition of the

respiration is practically never absent. Where there is a family history of asthma from childhood one may get benefit for two or three weeks and then bitter disappointment. In such, a mildly toxic dose has to be given. In difficult cases a mixture of peptones sometimes succeeds best.—A. G. Auld, *Brit. med. J.*, 1/1920, 568. See also *Serum Peptone*, p. 664.

### Technique.

Two distinct procedures have been evolved: (a) *Intravenous*; (b) *Intramuscular*.

### INTRAVENOUS TREATMENT.

A 5% solution of peptone, of a special type, is employed. It contains 85% protein, 60% of which represents primary and secondary proteoses in the proportion of 1 to 6, *i.e.*, there is a high content of the secondary bodies. The hydrolysis has not been carried to the amino-acid stage. It does not contain substances irritant to the tissues on injection. Care is taken (a) to prevent the delicate albumoses being decomposed by excessive heat, (b) to neutralise the solution; (c) to ensure that the solution is sterile. Contamination may cause grave consequences. The solution is in effect a culture medium for bacteria in the event of chance contamination.

Peptone is administered in a series of 10 graded doses:—

First	Dose 0.3 ml ( 5 minims).	Sixth	Dose 1.3 ml (20 minims).
Second	" 0.5 " ( 8 " )	Seventh	" 1.5 " (25 " )
Third	" 0.7 " (11 " )	Eighth	" 1.5 " (25 " )
Fourth	" 0.9 " (13½ " )	to	
Fifth	" 1.1 " (17½ " )	Tenth	" 1.5 " (25 " )

### CONTINUATION COURSE (INTRAVENOUS).

In addition to the above, a set of six doses is arranged as follows—Three doses each of 2 ml (30 minims) and 2.5 ml (40 minims).

The injection is given *slowly intravenously* in the arm, no after-dressing being necessary. The doses are administered every fourth or fifth day. The dose must be varied in certain cases.

### SHADING-OFF COURSES (INTRAVENOUS).

The procedure according to A. G. Auld (*Brit. med. J.*, 1/1925, 448) is safe.

Writing concerning the intravenous technique, this authority advises dosage up to the tenth dose as hitherto, and after the tenth dose cases are broadly divisible into three classes. In one class the patient is quite well, and usually expresses surprise at his condition; in another he is much better, but not yet quite well, and in a third he may be but little better.

In the *first* class, two additional doses of 2 ml approx. may be given and then there is a shading off to complete the treatment with the following weekly dosage: 1.5 ml, 1.2 ml, 1.0 ml, and 0.6 ml. This completes the course.

In the *second*, if the patient is standing the peptone well, the dose may be increased to 2 ml and 2.5 ml, employing the Continuation Course. Then there is a *weekly* reduction to complete the treatment, namely, with a dosage of 2.2 ml, 1.5 ml, and 0.9 ml. If, however, during the treatment the patient has an attack of asthma, reduce the dose considerably, say, to 1.5 ml. Continue with this for two or three weeks and then reduce to 1 or 0.6 ml.

In the *third* type of case Auld advises that peptone, dissolved in the serum from the patient's blood, be injected intravenously. *Vide Serum-Peptone*.

SHADING-OFF COURSES FOR CLASS I contain 2 ml., 1.5 ml., 1.2 ml., 1.0 ml., 1.0 ml., 0.6 ml., and for CLASS II contain 2.2 ml., 1.5 ml., 0.9 ml.

In children, where the attacks are of the clear-cut spasmodic kind, peptone is particularly useful. It is of most use intravenously. The initial dose should be small and carefully given, because the patient may be sensitive to the peptone and have an attack of sickness or more grave anaphylactic symptoms. More commonly when a large dose is being given the patient will immediately flush, feel uncomfortable, and be sick. Subsequent doses in such event must be given into the muscle or subcutaneously. The value of peptone when given in large doses to promote protein shock is not so certain nor so convenient for use as an intravenous dose of T.A.B. or the mixed coliform vaccine. A course of peptone usually consists of twelve doses given twice weekly, but there is no great harm, often great benefit, in giving the course for six months, the large doses being given at weekly intervals. Hundreds of injections given with no alarming results—with one exception.—Frank Coke, *Brit. med. J.*, 1/1928, 468.

Asthma in children.—Peptone and like compounds not advisable as they may lead to dangerous results in very hypersensitive cases.—W. R. F. Collis, *Lancet*, ii/1930, 567.

**INTRAMUSCULAR TREATMENT**

For intramuscular use the 7½% solution is used in the same range of ten doses (0.3 to 1.5 ml.), as also a Continuation Course (Intramuscular) of six doses, three of 2 ml. and three of 2.5 ml.

*Dosage for children*—The 7½% solution is also used intramuscularly, commencing with 0.3 ml. (5 minims).

Intramuscular technique is as efficacious as the intravenous in the majority of adult cases.

Adrenaline, which is of acknowledged utility in asthma, has been used satisfactorily in conjunction with the peptone treatment.

**Serum Peptone.**

The intravenous injection of peptone dissolved in a serum obtained from the patient has given good results in cases where peptone alone proved unsatisfactory.

Run 2 or 3 ounces of blood into a sterile 4-ounce glass tube, and allow to stand corked at room temperature till next day. Allow no food for 5 hours before bleeding, so that the serum is clear. Pipette off and add an agar solution made by mixing one part of agar with 1000 of saline well boiled. One volume of this is shaken with 4 volumes of serum, and the mixture incubated at 37° for an hour. Peptone powder (Armour No. 2) is added, preferably 2½ or 3%, increasing to 5%, and the mixture is incubated for a further hour. Phenol 0.5%, *vide infra*, mixed with about 15 minims of saline is then added in two portions with shaking.

To a patient with quiescent asthma this solution is given in 1½ ml. doses intravenously every 3, 4 or 5 days, increasing gradually to 3 or 4 ml.—A. G. Auld, *Brit. med. J.*, 1/1926, 732, 1/1927, 829.

In preference, the blood should be obtained just prior to an attack.

The following is now advised. Incubate the agar serum for about 2 hours at 37°. Then 4 ml. of a 30% peptone solution mixed with 2½ minims of phenol is added to each ounce of the agar serum.—*Brit. med. J.*, 1/1928, 171.

Chloroform (3 or 4 drops) now employed as a preservative instead of phenol, giving a clear mixture for a considerable time.—A. G. Auld, *Brit. med. J.*, 1/1929, 991.

**Peptone Injections in Vaccine Treatment.**

In vaccine therapy, as an aid to overcoming hypersensitiveness met with, especially in treating the arthritic group of infections, peptone (1 and 2% strength, intravenous) has been well spoken of.

A course of 10 injections intravenously is advised as follows—

On the first day 0.1 ml. of a 1% solution, on the second day 0.2 ml. of 2% solution, on the third day 0.4 ml. of 2%, on the fifth day 0.8 ml. of 2%, on the seventh day 1.4 ml. of 2%, and thereafter, at three or four day intervals, 1.8 ml., two or three times. Having reached 1.4 ml., a subcutaneous dose of vaccine can be given at the same time. This may be rather larger than the one the patient was sensitive to before treatment. No reaction, it is stated, will occur.—H. Warren Crowe, *Brit. med. J.*, 1/1923, 1046.

Peptone recommended for anaphylaxis in vaccine-therapy by L. Moinson *Lancet*, 1/1929, 1097.

**REFERENCES TO PEPTONE THERAPY**

**ASTHMA**—Treatment by desensitisation, though still empirical, has given very good results in some cases.—*Lancet*, 1/1931, 1140.

It is an undeniable fact that a small injection of animal protein in high dilution has very marked effect on the spasmodic attack associated with asthma.—T. Nelson and A. D. Porter, *Lancet*, 1/1931, 1344.

Asthma due to protein sensitiveness (dog). Opinion divided as to peptone.—C. J. Murphy, *Lancet*, 1/1931, 813. Asthma well treated.—J. Mowbray, *Lancet*, 1/1931, 813.

Eleven out of 20 bronchial asthma patients "more or less" improved with intravenous injections of a 5% solution, the doses increasing from 0.5 to 3 or 4 ml. The writer agrees with Dr. Auld that the intervals of recurrence of the attacks become less frequent after peptone therapy.—P. Boot, "The Treatment of Bronchial Asthma by Intravenous Injections of Peptone," Review, *Lancet*, 1/1926, 6.

**ARTHRITIS**.—Good results in rheumatic or fibrositic conditions and toxic states, e.g., urticaria. Contraindications: marked debility, tuberculosis, diabetes and advanced cardiovascular disease. Primary dose, 0.4 g. of peptone for a

man, 0.3 g. for woman, intragluteally with injections at 5 or 6 day intervals of twice preceding dose. Three or four injections usually effected cure. Dosage regulated to obtain reaction temperature of about 101°F.—E. Bulmer, *per Brit med J Ept*, 1/1925, 8.

Rheumatoid arthritis showed marked improvement from use of peptone — J. Eason, *Lancet*, 11/1926, 1065.

Arthritis deformans treated with peptone intramuscularly, 0.2 g dose weekly — Goodall, *Brit med J*, 1/1923, 512.

EPILEPSY.—Twenty cases of *haut mal* type (average age 18 years). Peptone intravenously arrested fits in 9 and lessened frequency in a further 6. (Bristol Royal Infirmary and Stoke Park Colony for mental defectives) — F. H. Edgeworth, *Brit med J*, 11/1920, 780. See also A. G. Auld, *ibid*, 840.

Intramuscular injections proved of great benefit in a man of 35 who had suffered from fits for 15 years. The first dose of peptone brought improvement. The full course of injections was given, terminating with the continuation course. Should be tried in resistive cases — G. R. Hull, *Practitioner*, 11/1922.

MIGRAINE.—In the treatment of migraine, resistant to the commoner methods, some cases (7 out of 20) showed marked improvement after 8 to 10 injections of a 5% solution, from 5 to 25 minims being injected at a time, each dose being increased by 5 minims — *Lancet*, 11/1927, 241.

Migraine successfully treated with peptone *per os*, 1 grain twice daily — *Brit med J*, 1/1930, 1159.

PNEUMONIA, SUBSEQUENT TO OPERATIONS INVOLVING THE UPPER ABDOMEN, thought to be anaphylactic in origin, the protein shock coming from the intestines. Desensitisation before the operation with peptone 0.3 g. in normal saline 2 ml. is now carried out when time permits in all abdominal sections and no case which has had peptone has developed pneumonia — M. Dixon, *Brit med J*, 11/1927, 985.

URTICARIA.—CHRONIC CASES OF URTICARIA, SEBORRHOEA, SEBORRHOIC ECZEMAS, DERMATITIS DUE TO IRRITANTS, AND CHRONIC SKIN CONDITIONS generally, where the patient is sensitised, are affections in which excellent results were obtained using peptone 5%, injected intravenously. It is essential to use a reliable brand of peptone and one that is histamine-free. In acute conditions the intramuscular injection of 5 ml. of the patient's blood, giving a further injection of 10 ml. five days later and continuing with this quantity at intervals of 5 days, seemed to give good results. The reduction of the pH value of the urine (if it is hyperacid) to normal by means of an alkaline mixture is also advocated — H. R. B. Hull, *J. R. nav. med. Serv.*, April, 1926, 147.

In military medical practice the method of value in cases of local sensitisation such as seborrhœic dermatitis that has been scratched and infected with a skin staphylococcus, and of general sensitisation such as urticaria. The graduated doses are "fool proof" and an overdose in a highly sensitive patient is impossible. They have a remarkable effect on most cases of asthma — J. R. *Army med Cps*, Nov. 1926, 400.

Urticaria has been treated with success by peptone *per os*. It is a manifestation of the anaphylactic state. French dermatologists advocate the ingestion of 0.5 g. of peptone one hour before each meal — R. Hallam, *Brit med J*, 11/1928, 880.

**Eupepton** (Allen & Hanburys, London). Therapeutic and bacteriological peptones. No. 1. For injection in non-specific protein therapy and for preparation of the culture medium for the Rideal-Walker test. No. 2. For preparation of culture media for general bacteriological purposes.

**Sterules Peptone** (Martindale, London). Ampoules of sterile peptone solution, 5% or 7½% strength, each strength being issued in 10 graded doses from 0.3 to 1.5 ml., also in doses of 2 and 2.5 ml. for the continuation course.

**Witte's Peptone**.—This brand of peptone is made at Rostock in Germany. It is much more toxic in effect. According to Auld (*Brit. med J*, 1/1921, 696) it contains too much primary proteose in relation to secondary (roughly 1 to 2), whilst in Armour's the proportion is 1 to 7.

Some cases of asthma and hay fever are remarkably sensitive to intravenous injection of Witte's peptone. 0.2 ml. of 2% solution caused vomiting, the patient's eyes became suffused, and in less than five minutes his back was covered with urticaria. — A. E. Gow, *Brit med J*, 11/1921, 237.

Histamine to extent of 0.00335 g. in 100 g. was found in Witte's peptone. Its presence in peptone is responsible for dyspnoea, flushing, etc., sometimes

produced. It is useless in the immunising process, if not actually harmful. Armour No. 2 peptone never gives the histamine effect. It may be safely given to young children. Witte's peptone is best given with a weaker peptone.

Physiological testing suggested. The dermal (scratch) test may give evidence as to the presence of histamine in a strong peptone solution. All individuals give a marked though varied response to extremely dilute histamine solutions. Ergamine can be used as control. Preparations giving a large wheal are unsuited. Confirm by intravenous injection of a small dose—A. G. Auld, *Brit. med. J.*, 1/1921, 698; 1/1922, 835.

Anaphylactic asthma successfully treated with Witte's peptone. Initially hypodermically 0.3 ml. of 2% solution, with sufficient sodium carbonate to suspend and neutralise it in normal saline, increased every fifth day by 0.2 ml. up to sixth injection (1.3 ml.), when symptoms disappeared, this dose repeated further three times and patient discharged cured.—*Indian med. Gaz.*, 1926, 285.

**"Peptone Witte Special 30."** Contains 14.87% total N (7.48% as albumose, 5.01% as peptones, 1.88% as amino-acids, remainder 0.5%).

Stated to be less toxic than Witte's ordinary peptone. Fatal dose 80 to 100 mg. per 100 g. rat, against 40 mg. 5% solution produces no irritation subcutaneously or intramuscularly, and is satisfactory intravenously, but the latter must be used rather cautiously. Results from Germany and elsewhere show that non-specific treatment may well replace specific, even if the allergen can be discovered. The proteose of the patient takes up the allergen and excretes it (Oriol), which alone is sufficient reason for injecting peptone.—A. G. Auld, *Lancet*, 1/1931, 804.

**ASTHMA.**—Among non-specific agents Witte's No. 30 peptone is probably the best. Tuberculin, milk and vaccines are in general a waste of time and money—G. W. Bray, *Brit. med. J.*, 11/1933, 45.

**Urinary Proteose.** Proteose in the urine excreted in anaphylactic and allied conditions. The substance gives the biuret reaction. It is not coagulated by heat, nor by half-saturated ammonium sulphate, but is coagulated by full saturation and by lead acetate. Gave intradermal reactions in dilution 1:100,000 in horse sensitives. The proteose contains the antigen to which the patient was sensitised. Used in urticaria, etc.—G. H. Oriol and H. W. Barber, *Lancet*, 11/1930, 231.

Injections of autogenous urinary proteose incredibly specific in conditions such as chronic urticaria, angioneurotic oedema, eczema, prurigo, dermatitis herpetiformis and psoriasis. Only infinitesimal doses necessary, e.g., 0.025 to 0.1 ml. of a dilution of 1 in 10 million, or even 1 in 100 million. Having found the dose on which patient improves progressively decrease rather than increase it.—H. W. Barber, *Lancet*, 11/1931, 1267.

"Specificity" questioned. Chief peculiarity not specificity, but property of producing intense local inflammatory reaction in certain individuals. The significance must be interpreted cautiously.—R. M. Lyon, G. H. Percival and C. P. Stewart, *Brit. med. J.*, 1/1932, 136.

Proteose is not a chemical substance but a more or less fortuitous collection of substances excreted by the kidneys. Proteose is present in all urines but the more ill the person the more there is likely to be present. It is always toxic, and injected into any man's skin, whether well or ill, will produce a wheal. The alleged specific reaction is a question of slightly more or slightly less than one gets in control cases and for a critical opinion great caution is necessary. An immunotherapy based on this alleged specificity has no scientific foundation.—John Freeman, *Lancet*, 1/1932, 561. See also *ibid.*, 570.

Treatment with proteose prepared from the patient's urine has given satisfactory results in chronic eczema and urticaria. 16% of normal persons and 67% of patients suffering from skin diseases gave positive reactions to their own proteoses.—Norman Burgess, *Brit. med. J.*, 1/1933, 916.

Further observations on the biochemistry of asthmatic conditions with special reference to the urinary proteose.—G. H. Oriol, *Lancet*, 11/1933, 406.

The proteose-like substances obtained by Oriol and Barber's technique from allergic and non-allergic patients and from normal persons appear to be indistinguishable. They are not antigenic and as therapeutic agents they are ineffectual—Cornbleet and Kaplan, *Arch. Derm. Syph.*, N.Y., Oct., 1934, 497.

## (2) Milk.

**Dose.**—5 to 10 ml. intramuscularly but much smaller doses have been used in certain affections.

(The milk in preference should be freed from the bulk of its fat.)

The gonococcus cannot resist a high temperature. It has been observed that if an intercurrent febrile disease arises whilst a patient is suffering from gonorrhoea, or an acute epididymitis complicates the case, the urethral discharge may cease without returning. Schmidt and Saxyl reported in 1916 that protein reactions could be produced by milk injections. Hence, these injections which have the power of raising body temperature might have effect on the gonococcus.

The method was tried in acute and subacute stages of gonorrhoea, injections into the gluteal muscles of sterilised milk in 5 ml. doses, 10 ml. into each buttock being given. Chill, general malaise and rise in temperature followed, normal in 24 hours. Dangers nil and results good.—M. W. Browdy, *Lancet*, 1/1923, 874.

ACUTE GONORRHOEA treated with milk injections combined with local treatment Initial dose 4 ml., increased by 2 ml. Duration of treatment shortened.—*Brit med. J. Epit*, ii/1924, 86

Milk injections in gynaecology.—*Brit. med. J. Epit*, i/1925, 13.

ERYSIPELAS.—Rapid recovery in 15 cases following intragluteal injection of 5 ml. Contraindications pulmonary tuberculosis and chronic recurrent hematemesia.—*Brit. med. J. Epit.*, i/1928, 85.

G.P.I.—Milk therapy considered superior to anti-syphilitic treatment. Injections of 10 ml. of sterilised milk under the skin of the abdominal wall. 40 cases of G.P.I., many of chorea, and several of epilepsy treated by this method in Budapest.—*Lancet*, i/1924, 1231.

INTERSTITIAL KERATITIS well treated with combined treatment of Neosalvarsan (intravenously) and milk (intramuscularly)—Van Lint, per *Prescriber*, 1923, 73.

LEPROSY well treated by intravenous milk injections. 12 cases treated with sufficiently good results to enable them to resume their employment. The treatment is drastic and dangerous and especially applicable to the late and more hopeless forms of the disease.—N. A. Dyce Sharp, *Trans R Soc trop. Med Hyg.*, Jan., 1928, 308

Aolan (*Beiersdorf, Welwyn Garden City*). Milk protein preparation for intramuscular injection in non-specific therapy

Caseosan (*Heyden, Dresden, Braun, London*). Sterile casein solution containing about 5% of casein. For subcutaneous, intramuscular or intravenous use in non-specific protein therapy.

Hypertherman (*Napp, London*). Milk protein with a strain of a saprophytic coli bacillus cultivated from milk. Dose.—From 2 to 5 ml. every third or fourth day intramuscularly continued for three months (combined with thyroid medication). In the treatment of obesity and for non-specific protein therapy

Sterules Milk (*Martindale, London*) contain 5 ml. or 10 ml. of sterile milk.

Xifal-Milk (*Napp, London*). Combination of sterilised milk and a vaccine of low virulence. Dose.—2 to 5 ml. intramuscularly. Non-specific protein therapy for the treatment of degenerative epilepsy and cerebral conditions of a traumatic, infectious, toxic or apoplectic aetiology.

### (3) Vaccines.

Various vaccines have been employed including *B. coli*, gonococcus, streptococcus and typhoid, of which the last-mentioned is the most popular. It is diluted with physiologic solution of sodium chloride until 1 ml. contains 100 million organisms, the initial dose for adults is from 10 to 25 million. Tuberculin has also been used, particularly in the treatment of asthma.

ARTHRITIS.—T.A.B. vaccine intravenously produces rapid improvement in 80 to 90% of cases, which is maintained in between 50 and 60%, the types responding best being acute and subacute, where disease is confined to the peri-articular tissues. Injections of no use unless all possible foci of infection removed. Reactions severe, but contraindications few—disease of myocardium, gross kidney disease, chronic alcoholism, tuberculosis and syphilis being the chief. Cases of the menopause group, of the chronic villous type and those showing achylia do not do well. Initial dose 100 million (in private practice 50 million), increased at each subsequent dose by 100 million, 4 days elapsing between injections. Dosage should be regulated to produce rigor, sharp rise of temperature, quick fall, and profuse perspiration. Of 50 cases treated 44 were discharged after 4 weeks as definitely improved.—W. Yeoman, *Lancet*, 1/1926, 1246-50; see also *ibid.*, 1265.

The results in rheumatoid arthritis from typhoid vaccine intravenously may be as much attributable to stirring-up of focus of infection as to stimulation of



the defensive mechanism of the body, and the ultimate factor in determining cure may be the response to the antigenic activity of the infecting organism, this response being evoked not directly but indirectly by the protein injected — E. M. Dunlop, *Brit. med. J.*, 11/1924, 1110

**ASTHMA** True cases of bronchial asthma benefited by prolonged injections of P.T.O. dilutions, beginning with 0.5 ml of 1 in 1,000,000 and gradually increasing. The treatment must be kept up for a year at least and injections twice a week are given for the first 4 months, then once a week for 4 months, and lastly once a fortnight — T. Nelson, *Practitioner*, 1/1927, 382

Tuberculin in treatment of asthma acts merely by virtue of its protein content — L. Hofbaver, *Prescriber*, 1926, 158

**CHOREA** — Treatment by pyrexia induced by intravenous injection of triple typhoid vaccine containing 1000 million typhoid and 750 million each of paratyphoid A and B per ml, beginning with 0.05 or 0.1 ml, the object being to attain a temperature of 104° to 105.5° and to maintain it for four hours. Treatment continued daily till choreic movements have disappeared — usually within a week. Now the routine procedure in the Children's Medical Service of the Bellevue Hospital, New York — D. Bateman, *Brit. med. J.*, 1/1933, 1003. See also J. W. Cheetham, *ibid.*, 1130

**GENERAL PARALYSIS** — Typhoid vaccine as a substitute for malaria therapy, q.v. T.A.B. containing 100 million *B. typhosus* and 750 million *B. paratyphosus* A and B, intravenously, 1 ml for 10 days, starting with 300 million total, and rising to 6000 then 6 weeks' interval and recommence with 1500 million, rising to 20,000 in 10 days, with 4 injections of neoarsphenamine in the interval. Remission induced. Contraindications — arteriosclerosis, pulmonary disease, myocardial and advanced cardiovascular disease, and marked focal infections — J. M. Mackenzie, *per Prescriber*, 1929, 302, *Lancet*, 1/1929, 288

**SCIATICA** of the sacro-iliac joint. T.A.B. vaccine intravenously gives the best chance of removal of symptoms in the shortest possible time — W. Yeoman, *Lancet*, 11/1928, 1119

**VASCULAR DISEASE** — One of the newer fields for foreign protein therapy is that of vascular disease, particularly thrombo-angitis obliterans, the pain of which is often excruciating, and Brown considers the intravenous administration of typhoid vaccine the best medical measure for its relief. Allen and Smithwick have reported successful results with typhoid vaccine in Buerger's disease, in the gangrene of arteriosclerosis, and in purely vasomotor types of vascular occlusion. These authors used doses of from 125 to 300 million bacilli but Wright believes that the chill should be avoided and recommends small doses just enough to produce 2 or 3 degrees of fever. Wright recommends an initial dose of 10 million typhoid bacilli, with an increase of 10 million with each subsequent injection. Goodman and Gottesman have also reported enthusiastically on the use of fever therapy in vascular disease, particularly Ravnaud's disease — R. L. Cecil, *J. Amer. med. Ass.*, 11/1935, 1852

**Omnadin** (*Bayer Products, London*) Compound sarcine vaccine containing albumins, lipoids and fats. Dose — 2 ml intramuscularly daily. Non-specific therapy in all fevers and in acne and furunculosis

**Pyripher** (*Haer Ltd, Basel, Yarrow, London*) Vaccine containing bacterial autolysates and dead bacteria from the coli group. For pyrexial treatment of paralysis, tabes, dementia præcox, etc., and as a substitute for malaria therapy. Ampoules contain graded doses for intravenous injection

**Vaccineurin** (*Napp, London*) Bacterial autolysate prepared from *S. pyogenes* and *B. prodigiosum*. Dose — 1 ml intramuscularly, a course consists of 18 injections at 2-day intervals. The bacteria used have strong neurotropic properties and the preparation is of value in neuritis, neuralgia, sciatica, etc.

#### (4) Artificially Induced Disease.

**GENERAL PARALYSIS TREATED BY MALARIA** — The principle is that remission in chronic disease may occur after an attack of acute specific fever. Subcutaneous injections are given of 2 to 4 ml of blood from the vein of a patient suffering from benign tertian malaria.

The donor's blood should be given before he receives any quinine. Onset and course of the inoculated malaria differs from ordinary tertian malaria, and as a rule after 4 or 5 attacks of tertian it becomes quotidian, with often high temperature. As little as 7 gr. of quinine bisulphate twice daily for 3 days and then once a day for 4 days will rid patient of malarial parasites. Then neoarsphenamine is given. — J. Gerstmann, *Brit. med. J.*, 11/1925, 481.

In treatment of general paralysis a rigor on alternate days is followed by greater benefit than a daily rigor. Allow the primary attack to go on 4 or 5 days then give 3 to 5 gr of quinine to check temporarily and wait for relapse. In this way the temperature is nearly always of the true tertian character with rigors on alternate days.—Leader, On Report of First Results of Laboratory Work on Malaria in England—Col S P James and P G Shute, *Brit. med J*, 11/1928, 79.

Watch should be kept for undue enlargement of spleen, especially if patient has previously had malaria.—N. G. Harris, *Lancet*, 11/1928, 500.

Allow at least 8 rigors. Malaria effectively cured by quinine. No relapses with inoculated malaria—compared with 50% relapses with mosquito bites. Follow up with 3 g of tryparsamide intravenously and 0.2 to 0.4 g of bismuth intramuscularly weekly in 10-week courses with intervals of 4 weeks.—R. Lees, *Brit. med J*, 11/1931, 338.

Ten years of malaria therapy results in 368 cases. It undoubtedly improves the bodily health, prolongs life to a marked degree in some 35% of cases, and has beneficial action on habits and cleanliness. In 18 to 20% it produces clinical improvement apparently lasting many years, and often allows resumption of healthy and useful home life.—J. E. Nicole and E. J. Fitzgerald, *Brit. med J*, 1/1934, 427.

RAT-BIT FEVER instead of malaria less weakening. Fever controlled by neorarsphenamine after 32 days. 2 deaths attributed to the treatment in 72 cases.—Per *Prescriber*, 1929, 301.

See also Oleum Sulphuris, p. 874.

#### (5) Blood and Sera.

Beneficial results obtained by autohæmotherapy in hyperchlorhydria, mucous-membranous enteritis, conjunctivitis, rhinitis, pharyngitis, bronchitis, leucorrhœa and non-specific urethritis. It has also proved of value in certain cases of gastric ulcer, especially during painful crises, in pellagra, herpes zoster and in depressive or melancholic psychoses.—F. Achitouv, per *Brit. med J. Fpit*, 1/1935, 73.

ASTHMA.—Twenty-four asthmatic children received 5 injections each of 10 ml of their own blood, which was withdrawn from the median basilic vein and injected immediately into the buttock, without admixture with citrate or separation of either plasma or serum. Observations over a period of 6 to 12 months afterwards indicated that in approximately three-quarters the frequency of attack was appreciably reduced and in every instance some alleviation of severity was manifest.—K. Maddox and R. F. Back, *Arch. Dis. Childh*, 1935, 380.

TYPHUS.—16 severe cases treated by intramuscular injection of 10 ml of the patient's blood. Each injection was followed by an immediate improvement in the general condition, and the duration of the disease seemed to be shortened by a series of 4 or 5 injections.—A. Babalian, per *Med. Annu*, 1935, 463.

WHOOPIING-COUGH.—After failure of vaccine therapy 20 severe cases in children aged from 25 days to 30 months in the paroxysmal stage were treated by one or two intragluteal injections of maternal blood, all but three showed rapid improvement.—V. de Gironcoli, per *Med. Annu*, 1936, 509.

**Antibacsyn** (*Antibody Products, Watford*). A preparation derived from ox serum, "consisting of a suspension in carbol saline of serum euglobulin adsorbed to the hydroxides of calcium and magnesium." For use wherever protein therapy has been found effective. *Dose*—1 or 2 ml subcutaneously.

**Antimalignyn** is an allied preparation suggested for use experimentally in the treatment of malignant disease.

**Edwenil** (*Spicer, Watford*). A polyvalent antibacterial agent, consisting of the antibacterial, heat-stable element from normal serum in 0.5% carbol saline. *Dose*—2 ml subcutaneously. Used in endotoxic infections, asthma, influenza, measles, mumps, otitis media, pertussis, etc. Contraindicated in conditions in which a sudden swelling might cause embarrassment, or an increase of secretion cause trouble (e.g., bronchitis with much secretion), also in cholecystitis and appendicitis.

**Globenil** is an allied preparation suggested for use experimentally in the treatment of malignant disease.

#### (6) Vegetable and Animal Proteins.

Hay fever and most forms of asthma are due to a peculiar reaction of the tissues ("anaphylaxis") of sensitive individuals to certain proteins which are inhaled in the air or swallowed with food. Some individuals are sensitive to

only one protein and others to a large number. The proteins to which sensitisation is most frequent are (1) pollen proteins, (2) epidermal proteins (from animal hair or feathers), (3) food proteins, and (4) bacterial proteins. It is frequently possible to determine by a cutaneous or, especially in the case of pollen sensitisation, by an ophthalmic reaction, employing test solutions of protein extracts, whether a patient is susceptible to a particular protein or group of proteins. In the skin test the protein extract is introduced either intradermally, by scarification, or by merely pricking the skin, using on an adjacent spot a control of normal saline, the areas usually chosen for the test being the forearm in men and the front of the thigh in women and children. In the case of a positive reaction a wheal will begin to appear within 5 minutes. The ophthalmic reaction consists in a slight reddening of the eye within 5 minutes of the instillation of a solution of a pollen extract into the conjunctival sac. The normal man never gives this reaction. The offending protein having been discovered the patient is then given a course of injections with the appropriate desensitising agent.

In the majority of asthmatics the trouble is due to inhalation of dandruff from fur, feather or hair of domestic animals—F. Coke, *Brit. med. J.*, 1/1921, 372 and 615. See also J. Freeman, *Practitioner*, 1/1926, 73; Mackenzie Wallis, *Brit. med. J.*, ii/1921, 796.

80% of asthmatics found to suffer from some form of allergy. Common moulds form allergens to which 50% of asthmatics are sensitive. 1 in 1,000,000 dilutions often have decided therapeutic effect. Allergen-free chambers used in treatment.—W. Storm van Leeuwen, *Brit. med. J.*, ii/1927, 344. While van Leeuwen finds that *A. fumigatus*, which flourishes extensively in kapok, is one of the chief causes of asthma in Holland, where most mattresses are stuffed with the material, F. Coke advises its use in pillows to replace feathers.—Leader, *ibid.*, 355. Strong support for van Leeuwen's work.—D. Kennedy, *ibid.*, 517.

If a patient is sensitive to feathers alone he will be relieved of his asthma if put on kapok bedding. The house dust of patients' own houses used for desensitising patients. Reactions with proteins are extraordinarily specific.—F. Coke, *Brit. med. J.*, ii/1927, 517.

In England, the true hay fever due to grass pollen is a hundred times more important than all the other pollen fevers together. Extracts from all the various grass pollens furnish one and the same antigen for purposes of desensitisation to hay fever.—J. Freeman, *Lancet*, 1/1933, 573.

From an allergic study of 262 cases of dermatoses, including eczema, urticaria, prurigo, dermatitis venenata, etc., it was concluded that intradermal tests were of little value in determining the cause; though positive reactions were frequently obtained they were rarely of practical significance. The indiscriminate subjection of patients with dermatoses to a large number of skin tests is not justifiable.—H. V. Mendelsohn, *Arch. Derm. Syph.*, N.Y., 1934, 845.

Over 90% of 961 patients treated for hay fever in 1932 and 1933 were cured or relieved by prophylactic subcutaneous injections of pollen antigens. A mixed standard preparation containing extracts of all pollens found to be pathogenic in Central Europe preferable to searching for some specific antigen—K. Hansen, per *Lancet*, ii/1935, 201.

The various regions of the body do not react alike to skin tests. The back reacts more strongly than the upper arm, the flexor surfaces than the extensor, the upper arm than the forearm. Hence in comparing results one must make sure that all tests were made on the same region of the body. For instance, one should not compare a test made on the back with one made on the forearm. As to the back itself, wheals induced four fingerbreadths below the spine of the scapula were only half as large as those produced in the region of the spine of the scapula itself.—W. Schmidt, *Klin. Wschr.*, 1935, 1, 378.

**Mixed Inhalants Solution** (Bencard, London). Proteins from feathers, animal hair, dust and orris root, with peptone. Also available without peptone. Adrenaline is also added to prevent a general reaction in sensitive patients. Available in two strengths, ordinary and continuation course. 10 ml. of the ordinary strength is usually sufficient for one patient.

**Pollacine** (Parke, Davis, London). A polyvalent grass-pollen vaccine. **Hip-paxine**, **Ovaxine**, **Galaxine** and **Ichthaxine** vaccines are also issued for the treatment of horse-sensitive, egg-sensitive, milk-sensitive, and fish-sensitive cases.

**Pollantin** (Schimmel, Leipzig; Willows, Francis, Butler & Thompson, London).

Serum obtained from animals which have been treated with a preparation of the pollen grains of *Gramineæ*. For use in the treatment of hay fever.

**Peptonum Bovinum.** *Syn.* BEEF PEPTONE, DIETETIC PEPTONE. Is prepared by the action of pepsin on minced lean beef. Occurs as a white or yellowish powder or scales. Administered as lozenges (5 grains), enema (2 to 4 ounces of 1 in 8 solution), or as Suppositorium Nutriens.

Peptone may be manufactured by digesting 1 kilo of beef with 10 litres of water (containing 4 g. of hydrochloric acid per litre) with pepsin 10 g. for 8 hours at 50° with frequent shaking. Termination of reaction shown by absence of precipitate with nitric acid on adding to a little of the filtered liquid. Evaporate 1 kilo yields 250 g. approximately.

**Peptonised Beef.** A chocolate-coloured paste, having a bitter taste and the odour of extract of beef, prepared by artificially digesting beef by means of acidified fresh gastric juice and concentrating the solution. It is sometimes added to beef tea, but is too unpleasantly bitter to be readily taken by patients.

**Peptonoids of Beef.** Lean beef, finely minced, 8 oz., pancreatin 60 gr., sodium bicarbonate 60 gr., water 1 pint. Digest 3 hours at 130° F. with constant stirring; neutralise with hydrochloric acid, boil, strain and press. As enema 1 ounce with normal saline 3 ounces, *p.r.n.*

**Carrick's Liquid Peptonoids** (*G. W. Carrick, New York; Brooks & Warburton, London*). A predigested food prepared from beef, milk and wheat, with wine. *Dose.*— $\frac{1}{2}$  tablespoonful at intervals.

**Panopepton** (*Fairchild Bros. & Foster, New York; Burroughs Wellcome, London*). A medicated wine prepared from beef and wheat.

Both the above may be dispensed by registered chemists without requiring a spirit licence to be taken out, providing it forms a constituent of a *bona-fide* medical prescription given by a duly qualified medical practitioner.

**Beef Peptone with Malt.** *Dose.*—2 to 4 drachms. A palatable nutrient.

## PREPARATIONS OF MEAT AND BLOOD

**Suppositorium Nutriens** (*B.P.C.*). *Syn.* SUPPOSITORYUM PEPTONI. Contains 75% of beef peptone with gelatin and water.

**Meat Extract** is the product obtained by extracting fresh meat with boiling water and evaporating. Contains not less than 75% of total solids. It should be practically free from albumin. The yield from meat is about 3%.

**Fluid Meat Extract** is identical with above prepared by Liebig's original process, except that it is evaporated at lower temperature and contains not more than 75 and not less than 50% of total solids.

**Meat juice** is the fluid portion of muscle fibre obtained by pressure or otherwise and may be concentrated at a temperature below the coagulation point of the soluble proteins. The solids contain not more than 15% of ash, not more than 2.5% of NaCl (calculated from total Cl), not less than 12% of N, not more than 4% or less than 2% of  $P_2O_5$ . The nitrogenous substances contain not less than 35% of coagulable proteins and not more than 40% meat bases.—Allen, 1914, Vol. VIII, p. 390.

**Restorative Essence of Beef** is made from fresh beef, freed from fat, finely chopped up—16 oz. mixed with distilled water 8 oz., add 5 drops of hydrochloric acid, and 60 gr. or less of salt, stir well and allow to macerate for 3 hours, strain. The product has an agreeable taste, and should be taken cold. *Dose.*—A wine-glassful or more (Ringer). It is also prepared *peptonised* by digestion with pepsin at the body temperature.

These are best freshly prepared for the patient, but may be preserved a reasonable time by addition of formalin or chloroform.

**Beef Extract Making.** The meat is cut up and all tendons removed. It is then minced and boiled. After settling, the soup is skimmed to remove the fat. Next it is filtered and evaporated to 25 Beaumé, and it then contains 16% moisture. The whole process takes 5 days, and 10 lbs. beef gives 1 lb.—*Brit. med. J.*, ii/1930, 617. See also *S. Back, Pharm. J.*, ii/1931, 361.

**Beef and Malt Wine.** Extract of beef 4 oz., extract of malt 8 oz., port wine 1 gallon (*Ph. Form.*). or a meat juice and liquid extract may be used instead of the solid extracts

A "beef and malt wine" should contain at least 0.18% of nitrogen, and phosphorus equivalent to 0.12% of phosphorus pentoxide. Of 12 samples examined none contained these amounts.—*Brit. med. J.*, 1/1924, 819.

"The Chemistry of Flesh Foods and their Losses on Cooking," by R. A. McCance and H. L. Skipp. *Spec. Rep. Ser. med. Res. Coun., Lond.*, No. 187, 1933.

**Bovril** (*Bovril Ltd., London*).

A combination of beef extract and finely powdered beef fibrin and albumen, used as a substitute for ordinary beef tea

**Brand's Meat Juice** (*Brand, London*)

A teaspoonful in a wineglassful of water is a useful tonic. Is prepared by cold process resulting in retention of full activity of juice of the raw beef

**Eatan** (*British Amino Products, Surbiston, Fasset & Johnson, London*)

An essence of beef, described as a liquefied form of liver and animal proteins

**Essence of Beef** (*Brand, London*)

A soft, transparent, amber-coloured jelly, prepared from beef by exhausting with tepid water. It is agreeable to the palate and stomach of a delicate invalid, is useful in allaying obstinate vomiting. It is best taken cold by teaspoonfuls. Similar essences are made from mutton and chicken

Meat jelly is suitable for ulcerated stomach. Gelatin is a powerful protein sparer, easily digested, and fixes a great deal of acid

**Ferrocarnis** (*Brand, London*)

*Dose*—One teaspoonful in water thrice daily with meals

Described as a flavoured solution of iron in organic combination with concentrated raw meat juice. An iron tonic food

**Somatose** (*Bayer Products, London*) Water-soluble meat albumoses

*Dose*—2 to 4 teaspoonfuls daily dissolved in water. **Iron-Somatose** contains 2% iron

**Trophonine** (*Reed & Carnrick, Jersey City, Coates & Cooper, London*)

Tonic food prepared from beef, malt, barley, milk and cocoa and containing 19.5% v/v of alcohol

**Albumen** (*B.P.C.*) *Syn.* EGG ALBUMEN, WHITE OF EGG. The liquid white of the egg of *Gallus bankiva* var. *domesticus* (*Gallinæ*). A nearly colourless or pale yellow fluid contained in a fibrinous network broken up by beating. Sp. gr. about 1.045. Contains 12% of protein, and is coagulated on heating to about 70°, or by adding alcohol. Is used as an antidote to poisoning by soluble salts of mercury and other heavy metals

A diet containing 66% of raw egg white produces a definite syndrome in experimental rats. The egg white was rendered harmless by heating in a moist condition for 3 hours at 80°, or by coagulating quickly at 65°, or by mild digestion with HCl, or pepsin and HCl, at pH 2.4. The condition of the rats was cured by giving 20% beef liver, but not by giving yeast or dried egg yolk.—H. T. Parsons, *J. biol. Chem.*, 1931, 92, 64

**Albumen Siccum** (*P. Ned. V.*) *Dose*—*Ad lib.*

Yellowish, transparent, horn-like flakes obtained by evaporating white of egg at not exceeding 50°.

**Soluble** in about 10 parts of water, producing a neutral solution. Insoluble in alcohol and ether.

**Incompatible** with mineral acids, alcohol, mercuric chloride, tannin-containing preparations

In hyperchlorhydria and in nervous disorders egg albumen is a food which binds and neutralises hydrochloric acid. Also used as a protective in colloidal solutions and as a foam stabiliser in some foaming contraceptives

**EMULSIFYING AGENT FOR ESSENTIAL OILS.** The following was found to be efficient: Egg albumen powdered 1, cream of tartar 4.—*Pharm. J.*, ii/1925, 521. Emulsifiers—J. Cofman-Nicoresti, *Pharm. J.*, ii/1926, 350, 369

**Albumin Water**, for infantile diarrhoea and invalids in general. White of 1 egg mixed with sterile water 8 oz, sodium chloride 5 gr or *q s* and a little whisky or brandy added

**Ovi Vitellus**, yolk of egg, has a slightly alkaline reaction and consists of about 50% of water and 20% of oil emulsified by about 7% of lecithin and 15% of vitellin. An emulsifying agent giving emulsions not readily broken by acids or other electrolytes

**Albumin Sanguinis.**

*Dose*—*Ad lib* Made by inspissating blood serum Brown horn-like scales, not so soluble in water as egg albumen

**Hæmoglobin.** *Dose*.—5 to 30 grains (0.3 to 2 g.) or more

The principal constituent of red blood corpuscles. Is supplied commercially in reddish-black powder or in scale form consisting of the oxygen compound, oxyhæmoglobin. Is a combination of the protein, globin, with hæmatin,  $C_{34}H_{30}O_4N_4Fe \cdot OH$ ; pure hæmoglobin contains about 0.34% Fe, 16% N and 0.6% S. May be given according to condition in cachet, capsule, or mixed with wine. It is useful in ordinary secondary anæmia. Hæmoglobin solution gives a characteristic absorption spectrum (*Cf* Vol II for estimation in the blood and further details)

In the arterial circulation, hæmoglobin is present as oxyhæmoglobin (brilliant red in colour) the oxygen of which is given up to the tissues in its course, returning de-oxygenated (dark red) to the lungs by the venous system, where it is ready to take up fresh oxygen and so continue the process

**Hæmoglobin Capsules.** Contain 5 grains (0.3 g.)

**Elixir Hæmoglobini (B.P.C.)** *Dose*—1 to 2 drachms (4 to 8 ml.) Contains 10% w/v of hæmoglobin (about  $5\frac{1}{2}$  gr per drachm). An agreeably flavoured preparation of hæmoglobin as hæmatine

**Elixir Hæmoglobini cum Ovocithino.** *Dose*—1 to 2 drachms (4 to 8 ml.) As above with 3 gr of ovocithin per drachm added

**Hemoplas (Lumière, Lyons, Anglo-French Drug Co, London)** "Hæmoglobin in its natural state" Supplied in ampoules and dragees. In anæmia, hæmorrhage, tuberculosis, etc

**Chlorophyll (B.P.C.)** The green colouring matter of plants extracted first by ether, then alcohol—in which latter the chlorophyll is soluble, leaving the waxy matter behind, or it can be produced by acetone extraction. Supplied commercially in solid extract and liquid form. Oil soluble, alcohol soluble and water soluble varieties are available. Oil soluble chlorophyll is obtained by diluting the purified extract with a fat, alcohol soluble chlorophyll is obtained by dilution with castor or other oil, and the water soluble variety by the action of dilute alkalis on the purified extract. Is stated to possess blood-forming properties, especially in conjunction with iron. Further information on chlorophyll, see *Phyllosan*, Vol II

**Medulla Rubra (B.P.C.)**

*Dose*—20 to 40 grains (1.3 to 2.6 g.).

The mixed fatty material from the bones of calves and young oxen. Contains erythroblasts from which the hæmoglobin-containing cells of the blood are developed. The bone marrow of older animals is yellow and contains no erythroblasts. Has been used in various forms of anæmia.

**SECONDARY ANÆMIA** Desiccated red bone marrow and spleen, in equal proportions, given thrice daily in 5-grain doses, gave very definite improvement

in 41 out of 46 cases. Treatment continued for 6 or 8 weeks.—*Brit. med. J. Epit.*, 1/1925, 17. But not of value in pernicious anæmia.—*Prescriber*, 1926, 228.

PULMONARY TUBERCULOSIS improved by treatment with spleen extract and bone marrow, which definitely increased production of erythrocytes and hæmoglobin.—*Per J. Amer. med. Ass.*, ii/1925, 1513.

**Extractum Medullæ Rubræ (B.P.C.).** *Syn.* GLYCERIN EXTRACT OF RED BONE MARROW. *Dose.*—1 to 2 drachms (4 to 8 ml.).

1 in 4, in glycerin and chloroform water.

**Marrubin (Martindale, London).** A thick brown liquid made by extraction of veal-bone marrow. *Dose.*—1 to 2 drachms, increased if desired.

For the treatment of anæmic conditions. Also available in combination with pepsin, pepsin and quinine, bismuth and pepsin, bismuth and iron, [P1] bismuth and strychnine ( $\frac{1}{20}$  gr. per dr.), cascara, Tinctura Laxativa, podophyllin, hypophosphites, [P1-S1] ferric phosphate and arsenic trioxide ( $\frac{1}{100}$  gr. per dr.).

**Virol (Virol Ltd., London).** A preparation of bone marrow with malt, egg, and lime. Has nutrient properties for infants.

**Bynotone (Allen & Hanburys, London)** A combination of halibut-liver oil, bone marrow, yeast extract, hæmoglobin, malt extract and vitamin D. In malnutrition, pregnancy and convalescence.

## PHENACETINUM

*B.P., P. Helv. V, P. Belg. IV, P. Ned. V, P. Austr., P. Dan., P.G. VI.*

$\text{CH}_3\text{CO}\cdot\text{NH}\cdot\text{C}_6\text{H}_4\cdot\text{OC}_2\text{H}_5[\text{CH}_3\text{CO}\cdot\text{NH}:\text{OC}_2\text{H}_5 = 1:4] = 179\cdot1.$

*Syn.* ACETPHENETIDIN, ACETPARAPHENALIDE, ACETOPHENETIDINUM (*U.S.P. XI*), OXÉTHYLPARA-ACÉTANILIDE (*Fr. Cx.*), ACÉTYL-PHENETIDIN (*P. Ital. V*), FENIDINA, FENINA (*F.E. VIII*).

*Dose.*—5 to 10 grains (0.3 to 0.6 g.), in cachets, tablets, or suspended in mucilaginous fluids. *P.G. VI* has max. single dose 15 grains; max. during 24 hours 45 grains, approx.

An acetyl compound of phenetidin,  $\text{C}_6\text{H}_4(\text{NH}_2)\text{OC}_2\text{H}_5$  (the ethyl ether of *p*-aminophenol). It is analogous to acetanilide (antifebrin). White, shining, laminar, tasteless crystals, m.p.  $134^\circ$  to  $136^\circ$ . Soluble sparingly in water, about 1 in 1700, 1 in 21 of alcohol 90%; also soluble in ether, chloroform and in sulphuric acid without colour.

Does not liquefy with sodium salicylate, but phenazone does, e.g., phenacetin 10 gr., caffeine citrate 2 gr., sodium salicylate 5 gr., are not incompatible.

**Antidotes.** Treat as for poisoning by acetanilide, *see* p. 2.

**Uses.** Reduces temperature and soothes pain, very rarely causes rash or cyanosis. Successful in rheumatism, neuralgia, migraine and hysteria. In first stage of influenza relieves headache and mitigates aching of limbs. The safest of the antipyretics.

Antipyretic effect of phenacetin is enhanced by magnesium oxide in proportions of phenacetin 2 : magnesium oxide 1. Probable synergistic action.—*J. E. Winter and co-workers, J. Pharmacol.*, 1930, 347.

**Mist. Phenacetin. Co. (N.I.F.).** Phenacetin 5 gr., caffeine citrate 1 gr. compound powder of tragacanth  $7\frac{1}{2}$  gr., oil of cassia  $\frac{1}{2}$  m., water to  $\frac{1}{2}$  oz.

**Phenacetinum Effervescens (B.P.C.).**

*Dose.*—1 to 2 drachms (4 to 8 g.). About 1 in 20.

**Phenacetinum cum Caffeina Effervescens (B.P.C.).**

*Dose.*—1 to 2 drachms (4 to 8 g.). About 1 in 20 of phenacetin and 1 in 60 of caffeine citrate.

**Tabellæ Phenacetini (B.P.C.)** contain 5 gr. (0.3 g.).

**Tabellæ Phenacetini Compositæ (B.P.C.).**

*Dose.*—1 or 2 tablets. Phenacetin 4 gr. and caffeine 1 gr.

**Tabellæ Phenacetini et Caffeina Citratis (B.P.C.).**

*Dose.*—1 or 2 tablets. Phenacetin 4 gr. and caffeine citrate 1 gr.

**Dr. Faivre's Cachets (P. Basset, Paris; Wilcox, Jozeau, London).** Contain oxyquinothine 0.2 g., phenacetin 0.3 g., and magnesium oxide 0.1 g. (They no longer contain anudopyrine).

**Iminol (Boehringer, Mannheim; Pharmaceutical Products, London).** Lactyl-phenetidin (P.G. VI) in 7½ gr tablets. *Dose*—1 tablet several times daily, maximum daily dose 75 gr. Febrile conditions, insomnia in children, rheumatism, neuralgia, migraine.

**Kephaldol (Sangers, London)** Tablets containing phenacetin 2.15 gr., sodium salicylate 1.75 gr., quinine 0.45 gr., caffeine 0.25 gr., salicylic acid 0.15 gr., citric acid 0.25 gr. Analgesic and antipyretic.

[P. 81] **Treutabs (Homburg Pharma, London).** Tablets containing phenacetin 0.25 g., aspirin 0.125 g., codeine phosphate 0.01 g., Homburg salt 0.07 g. *Dose*—1 or 2 tablets—not more than 8 in 24 hours. Analgesic in all painful and febrile conditions.

**Phenocolli Hydrochloridum.** *Syn.* AMINOACETO-*p*-PHENETIDIDE HYDROCHLORIDE.

$\text{CH}_3(\text{NH}_2)\text{CO}\cdot\text{NH}\cdot\text{C}_6\text{H}_4\cdot\text{OC}_2\text{H}_5\cdot\text{HCl} = 230.6.$

*Dose.*—8 to 15 grains (0.5 to 1 g.).

A white crystalline powder with sharp saline taste, made by the action of ammonia on bromophenacetin. Soluble about 1 in 16 of water.

Useful in rheumatoid arthritis, especially in conjunction with piperazine. Also in influenzal neuralgia and headaches. Has been given in pertussis (½ gr. hourly).

**PHENAZONUM**

*B.P., U.S.P. XI, Fr. Cx., P.G. VI, P. Ned. V, P. Helv. V, P. Dan., etc.*

$(\text{CH}_3)_2\text{N}\cdot\text{C}(\text{CH}_3) : \text{CH}\cdot\text{CO}\cdot\text{N}(\text{C}_6\text{H}_5) = 188.11.$

*Syn.* ANALGÉSINE, ANTIPYRIN, DIMETHYL OXYQUINIZINE, PHENYL-DIMETHYL-ISO-PYRAZOLONE, 1-PHENYL-2 : 3-DIMETHYL-5-PYRAZOLONE.

*Dose.*—5 to 10 grains (0.3 to 0.6 g.) in cachets, tablets or solution. *U.S.P. XI* average dose 5 grains. Hypodermically 4 grains (0.25 g.) is painful. Has been given with cocaine hydrochloride ½ gr.

In white, crystalline, bitterish scales or powder, m.p. 111° to 113°. Gives a deep red colour with ferric chloride, nearly discharged by dilute sulphuric acid.



**Soluble** 1 in 1·2 of water, about 1 in 1·3 of alcohol 90%, 1 in 1·3 of chloroform, and 1 in 50 of ether.

**Incompatible** with spirit of nitrous ether, or other nitrites in the presence of free acid, an apparently inert bluish-green iso-nitroso-antipyrin being formed, also with the cinchona alkaloids, forming a precipitate which is soluble in weak acids

Further, with phenol, tannic acid, iodine or mercuric chloride (precipitates); amyl nitrite, ammonia alum, hydrochloric acid, calomel, ferric chloride, ferrous and ferric sulphates, cupric sulphate, nitrous acid, sodium bicarbonate or orthoform

Liquefies with butylchloral hydrate, betanaphthol and sodium salicylate, but solutions with the latter keep if dilute

**Antidotes.** Treat as for poisoning by acetanilide, *see* p 2

**AGRANULOCYTOSIS** In the recorded cases of agranulocytosis in which an analgesic drug has been suspected, an amidopyrine preparation has nearly always been held responsible. In view of the occurrence of cases following the use of Novalgin, it is important to bear in mind the possibility of antipyrine preparations being responsible when the causation of a case of agranulocytosis is under consideration. There are a number of proprietary preparations on the market containing antipyrin—C P Donnison, *Brit med J*, 1/1936, 84

**Uses.** It is an analgesic and antipyretic and is therefore of value in pneumonia, pleurisy, phthisis and erysipelas. In doses of 4 to 15 grains it relieves locomotor ataxy, chorea, migraine, facial neuralgia, rheumatism, sciatica and sea-sickness. Hypodermically for lumbago, sciatica, angina pectoris, biliary and renal colic, and dysmenorrhœa. A skin rash has at times been observed after its use, and in the past some poisonous effects were reported. A solution applied locally is hæmostatic. Local hæmorrhage of hæmophilia has been treated by application of a strong solution of antipyrin in ferric chloride

In middle-ear diseases, otitis media and inflammation of the tympanum, and tympanic membrane, a 5% solution in glycerin is used by instillation

**GLOSSOPHARYNGEAL NEURALGIA** well treated by phenazone and gelsemium—J P Martin, *Brit. med J.*, 1/1931, 533

**SCIATICA** The following relieves the painful symptoms—Phenazone 6 gr., phenacetin 3 gr., methylacetanilide 1½ gr., potassium sulphate 1½ gr., Dover's powder (*sine ipecacuanha*) 3 gr. To be given in a cachet 3 or 4 times in the 24 hours. Good effects are also obtained from the following—Phenazone 5 gr., phenacetin 5 gr., opium powder ½ gr., in a cachet, 3 to 6 of which can be taken each day.

Antipyrin (4 g in 10 ml of water with a little procaine hydrochloride) by perineural injection also alleviates pain—*Practitioner*, 1/1925, 382

**Mist. Phenazon. Co. (N.I.F.).** Phenazone 5 gr., potassium bromide 7½ gr., solution of burnt sugar 5 m, sodium salicylate 5 gr., aromatic solution of ammonia 15 m, water to ½ oz

**Phenazonum Effervescens (B.P.C.)** *Syn.* EFFERVESCENS ANTIPIRYN. *Dose.*—1 to 2 drachms (4 to 8 ml.). About 1 in 12

**Phenazonum cum Caffeina Effervescens (B.P.C.).** *Dose.*—1 to 2 drachms (4 to 8 g.). Contains about 1 in 12 of phenazone and 1 in 60 of caffeine

**Phenazoni et Caffeina Citras.** *Syn. and Prop. Name* ANTIPIRYN CAFFEINO-CITRICUM (*P. Austr.*, *P. Jap. IV*, *P. Helv V* and *P. Ned V*), MIGRAININE (*Bayer Products, London*).

**Dose.**—8 to 15 grains (0.5 to 1 g.). Contains phenazone 90%, caffeine 9% and citric acid 1%. Soluble 1 in 2 of water.

**Incompatibles** as phenazone *q.v.* Is serviceable in headache, but apt to cause sleeplessness

**Pommade Reclus.** *Syn* POMMADE ANTISEPTIQUE DE RECLUS (*Fr Cx. Supp.*, 1926), POMATUM ANTIPYRINI COMPOSITUM Phenazone 25, mercuric chloride 0.1, phenol 2.5, salol 6, iodoform 5, boric acid 15, alcohol 60% 65, soft paraffin 1000. The formula is often modified, it may be diluted or made stronger For burns [*P1*] 1.2% of orthocaine may be added

**Tabellæ Phenazoni** (*B P.C.*) Contain 5 gr (0.3 g.)

**Phenazoni Acetylsalicylas.**

$C_{11}H_{12}ON_2, CH_3CO_2C_6H_4COOH = 368.2$  *Syn.* ANTIPYRIN ACETYSALICYLAS

**Dose**—8 to 15 grains (0.5 to 1 g.)

A white crystalline powder, soluble 1 in 160 of water, but about 1 in  $3\frac{1}{2}$  of alcohol 90%. Analgesic, antipyretic and anti-arthritis, used in sciatica, hemicrania, influenza, etc

**Phenazoni Salicylas** (*B P C*)

$C_{11}H_{12}ON_2, C_6H_4(OH)(COOH) = 326.2$  *Syn* ANTIPYRINUM SALICYLICUM (*P Austr*, *P Belg*, *Fr Cx*, *P Helv V*, *P. Dan*, *P. Jap*, *P.G VI*, *P. Ned V*), SALIPYRIN, PYRAZOLONUM PHENYLDIMETHYLICUM-SALICYLICUM

**Dose**—5 to 20 grains (0.3 to 1.2 g.) Max single dose 2 g., max in 24 hours 6 g

A white crystalline powder, with sweetish taste, soluble 1 in 240 of water, 1 in 4 of alcohol 90%; incompatible with acids, alkalis and nitrites

Useful in acute rheumatic fever and in chronic rheumatism, and sciatica, also for influenza and any acute catarrh and for menorrhagia, as antipyretic in dose double that of phenazone.

**Dismenol** (*Madlener-Gavin, Genf, Roberts, London*) Tablets containing *p*-sulphamidobenzoic acid 0.05 g, phenazone 0.25 g, lactose 0.25 g **Dose**—1 tablet 2 or 3 times a day For dysmenorrhœa

[*P1 81 84*] **Disulphamin** (*Biochemical Laboratories, Locarno, Coates & Cooper, London*) Dimethylaminoantipyrinbismorphate 14%, with a compound of sodium nucleinate and hexaminesulphosalicylic acid **Dose**—The contents of a capsule (7½ gr) are dissolved in half a glass of cold water, 2 capsules taken every 2 hours until the contents of 12 to 14 have been taken Repeat on following day or days if necessary In influenza, pneumonia, acute rheumatism, etc Also used as an ear douche (2 capsules in 2 oz glycerin and 2 oz water) in otitis media, and as a gargle in tonsillitis, etc.

**Felsol** (*British Felsol, London*) Composition stated to be phenazone 0.47, phenyldimethyl-iodopyrazolone 0.03, antipyrine acetosalicylate 0.4, caffeine 0.1, Ext Visci Alb. 0.01 and Ext Brachycladus 0.01. As a prophylactic and remedy for asthma, also in angina pectoris, the dyspnoea of phthisis, and chronic bronchitis Makers state it can be used in cases of cardiac affections and is not cumulative **Dose**—First week 1 powder thrice weekly an hour after meals. Second week 1 powder night and morning Third week 1 powder every morning For children from 2 to 10 reduce to ¼ or ½ dose. Place powder on tongue and swallow with drink of water.

**Quadronal** (*Asta, Brackwede, Pharmaceutical Products, London*). A preparation containing phenazone, lactyl-*p*-phenetidin, phenacetin, magnesium peroxide and caffeine Analgesic and antineuralgic Tablets contain 7½ gr. **Dose**—2 tablets thrice daily

[*P1 81 84*] **Quadro-Nox** (*Asta, Brackwede, Pharmaceutical Products, London*). 9-gr. tablets containing barbitone 7½ gr and Quadronal (*sine* caffeine) 1½ gr. **Dose**—1 tablet at bedtime Hypnotic in nervous insomnia.

**Saridone** (*Hoffmann-La Roche, London*). Tablets containing phenyldimethylisopropylpyrazolone  $1\frac{1}{2}$  gr., phenacetin  $2\frac{1}{2}$  gr., caffeine 1 gr. *Dose*.—1 to 3 tablets 3 or 4 times daily. Analgesic and antipyretic.

**Sedonan** (*Napp, London*). 5% solution of phenyldimethylpyrazolone in glycerin. For instillation in otitis media, otalgia and other inflammatory ear conditions.

[P1 81-84] **Amidopyrina** (B.P.).  $C_{11}H_{11}(N[CH_3]_2)_2N_2O = 231.2$ . *Syn. and Prop. Name*. 4-DIMETHYLAMINO-1-PHENYL-2 : 3-DIMETHYL-5-PYRAZOLONE, DIMETHYLAMINOPHENAZONE, PHENYLDIMETHYLDIMETHYLAMIDOISOPYRAZOLONUM (*P. Ital. V*), DIMETHYLAMINOANTIPYRINUM (*Fr. Cx., P. Helv. V, P. Dan.*), AMINOPYRINA (*U.S.P.XI*), AMIDOFEBRIN, PYRAMIDON (*Bayer Products, London*).

[P1],[81] and [84] "*Amidopyrine; its salts.*"

*Dose*.—5 to 10 grains (0.3 to 0.6 g.). *Fr. Cx.* has max. single dose 15 grains; max. during 24 hours 45 grains approx. *P. Helv. V* max. per day 15 grains. *U.S.P. XI* average dose 5 grains.

A white powder with m.p.  $108^\circ$ . Soluble about 1 in 18 of water and 1 in 2 of alcohol 90%; readily soluble in ether, chloroform and benzene.

**Incompatible** with amyl nitrite, apomorphine and acacia.

**Antidotes**. Treat as for poisoning by acetanilide, *see* p. 2.

Amidopyrine and amidopyrine-containing preparations considered as ætiological agents in the causation of agranulocytosis. 172 cases cited in which the illness has definitely followed the use of these substances—R. R. Kracke and F. Parker, *J. Amer. med. Ass.*, ii/1935, 960. Amidopyrine in any form should no longer be used when other equally effective drugs are available, and it should be ordered only by a non-repeatable prescription—*Lancet*, ii/1935, 894. Since May 1933 no less than 128 cases have been reported in which agranulocytosis developed after therapeutic doses of amidopyrine; 70 of them were fatal.—P. Plum, *Lancet*, i/1935, 14.

A study of the acute intoxication of dogs by amidopyrine and benzene has shown that the effects are similar, and are antagonised in both cases by phenobarbitone. Clinical experience has shown, however, that agranulocytosis can be caused by combinations of amidopyrine with barbiturates, a form of conjoint therapy particularly popular at present. Barbiturates therefore inhibit the acute toxic actions of amidopyrine, but not the chronic toxic effects. The combination of amidopyrine with barbiturates appears thus to possess certain peculiar dangers, because the latter are likely to mask any immediate effects of overdosage with amidopyrine.—Danielopolu and co-workers, *Brit. med. J.*, ii/1935, 1108.

**Uses**. Antipyretic; similar to phenazone, but effective in smaller doses; of special effect in sciatica. Has been advocated for the treatment of measles (for dosage *vide infra*).

**INFLUENZA IN CHILDREN** well treated by giving a 3 or 4% solution. From birth to 1 month 0.05 g., 3 to 6 months 0.1 g., 6 to 12 months 0.15 g., 2 to 5 years 0.2 g. Given 2-hourly till temperature reached normal, then 3-hourly, then 4-hourly, and later 3 times daily. No unpleasant symptoms and temperature,

fell after third or fourth day.—G. Petrányi, *Amer. J. Dis. Childh.*, Dec., 1933, 1011, per *Brit. med. J. Ept.*, 1/1934, 46.

MEASLES well treated. *Dose*.—2 to 5 grains in teaspoon with a little water. 12 powders at 4-hourly intervals day and night. Completely aborts if given early, —J. I. Collier, *Brit. med. J.*, 1/1930, 1093.

See also G. H. Urquhart and A. H. Winchester, *Brit. med. J.*, 1/1930, 1153. H. B. Gladstone, 1198.

150 cases. 1 grain for each year of age, with a maximum of 5 grains. Temperature drops to normal within 24 hours, with improvements in general condition. Given 4-hourly day and night until temperature settled.—G. W. Ronaldson and J. I. Collier, *Brit. med. J.*, 11/1930, 995. On the other hand, W. H. W. Attlee treated 120 cases on "ordinary" lines against 9 with amidopyrine, and was not favourably impressed.—*Ibid.*, 996. Definitely good from 1 to 9 years, but over 12 it is not indicated.—H. G. Gladstone, *Brit. med. J.*, 11/1930, 1103. The boys in an epidemic with it were more comfortable and seemed less ill.—G. E. Friend, *Brit. med. J.*, 1/1931, 33. Effective. Apparently specific.—T. Pires, *Brit. med. J.*, 1/1931, 734.

Results in 194 cases, one half of which were treated by amidopyrine while the other half served as controls. The morbidity, fever, and complications were about equal in each group, and the drug did not prevent the appearance of the rash.—M. P. Barovsky and F. Steigmann, *J. Amer. med. Ass.*, 1/1933, 1859.

[P1 81 84] *Tabellæ Amidopyrinæ* (B.P.C.) contain 5 gr. (0.3 g.).

[D P1 81 84] *Tabella Amidopyrinæ Composita* (L.H.). Amidopyrine 4 gr. acetylsalicylic acid 5 gr., diamorphine hydrochloride  $\frac{1}{2}$  gr., carmine q.s. in 1 tablet.

[P1 81 84] *Amidopyrinæ Camphoræ*. *Dose*—5 to 10 grains. Used to diminish the sweats of phthisis.

[P1 81 84] *Amidopyrinæ Salicylæ*. White crystals. Analgesic for neuralgia and rheumatism. Tablets contain 5 gr.

[P1 81 84] *Amidophen* (Lilly, London). Capsules containing amidopyrine, phenacetin, caffeine, and hyoscyamus extract. Analgesic, sedative and antipyretic.

[P1 81 84] *Asciatine* (Pharmaceutical Specialities (May & Baker) Ltd., London). Chemical compound of amidopyrine and butylchloral hydrate in 4-gr. tablets. In neuralgia and insomnia due to pain. *Dose*.—For children 1 or 2 tablets, for adults 1 to 3.

[P1 81 84] *Compral* (Bayer Products, London).  $7\frac{1}{2}$ -gr. tablets containing amidopyrine combined with trichlorethyl-urethane for use in dysmenorrhœa and pain generally. *Dose*.—1 or 2 tablets 3 times daily before meals. A rapidly acting, mildly sedative analgesic.

[P1 81 84] *Gardan* (Bayer Products, London). A combination of amidopyrine and Novalgin in 5-gr. tablets. *Dose*.—5 grains (1 tablet) 2 or 3 times daily as an antipyretic and analgesic.

[P1 81 84] *Melabon* (Reutschler, Laupheim; Coates & Cooper, London). Oxyethylacetanilide, phenylamidourea-amidopyrine, phenazone, caffeine citrate, lithium carbonate, calcium phosphate, calcium sulphate, magnesium phosphate, sodium phosphate and silica. Supplied in cachets as an anodyne and sedative for the alleviation of painful symptoms of every kind.

*Novalgin* (Bayer Products, London). Sodium phenyldimethylpyrazolon-methylaminomethanesulphonate in 5-gr. tablets. *Dose*—1 tablet 3 or 4 times daily after meals, with water.

An amidopyrine derivative introduced as an anti-rheumatic, stated to be better tolerated and more effective than salicylates, for use in articular and muscular rheumatism, sciatica, polyarthritis, and lumbago.

An injection of 1 to 2 ml. of 50% Novalgin solution, available in ampoules, is also given as an analgesic.

[P1 81 84] *Sinepan* (Richter, London). Amidopyrine 0.2 g., codeine hydrochloride 0.025 g., narcotine hydrochloride 0.025 g. *Dose*.—1 or 2 tablets thrice daily. Substitute for morphine and opium preparations.

[P1 81 84] *Trigemin* (Bayer Products, London). Combination of amidopyrine and butylchloral hydrate. *Dose*.—0.25 to 0.5 g. Analgesic.

## PHENOL

*B.P., U.S.P XI, P. Dan., P. Helv. V.*

$C_6H_5 OH = 94.05$ .

*Syn* ACIDUM CARBOLICUM, PURE CARBOLIC ACID, PHENYL HYDRATE, BENZOPHENOL (*P. Belg. IV*), FENOL (*F.E. VIII*)

[P1] "*Phenols (any member of the series of phenols of which the first member is phenol, and of which the molecular composition varies from member to member by one atom of carbon and two atoms of hydrogen) except in substances containing less than 60% weight in weight, of phenols, compounds of phenol with a metal, except in substances containing less than the equivalent of 60% weight in weight, of phenols.*"

[P2] "*Phenols as defined in Part I of this List (see [P1] above) in substances containing less than 60% weight in weight, of phenols, compounds of phenol with a metal in substances containing less than the equivalent of 60% weight in weight, of phenols*"

[33] "*Phenols—in Carvacrol, coal tar, crude or refined, cresote obtained from coal tar, essential oils in which phenols occur naturally; medicines containing less than 1% of phenols, nasal sprays, mouth-washes, pastilles, lozenges, capsules, pessaries, ointments, or suppositories containing less than 2.5% of phenols, smelling bottles; soaps for washing, solid substances containing less than 60% of phenols, tertiary butyl cresol, thymol*"

[36] "*Phenols—specify proportion as the proportion of phenols (added together) contained in the preparation*"

"*Compounds of phenol with a metal—specify as the proportion of phenols (added together) that the preparation would be calculated to contain on the assumption that the compounds of phenols with a metal had been wholly converted into the corresponding phenols*"

*Dose.*—1 to 3 grains (0.06 to 0.2 g). *Fr* Cx max. single dose  $1\frac{1}{2}$  grains; max. during 24 hours  $4\frac{1}{2}$  grains approximately *U.S.P XI* average dose 1 grain.

In colourless crystals or agglomerated masses liable to become pink—a little sulphurous acid will prevent this for a long time. Neutral to test paper; made by distillation of coal tar. *M.p.* 39° to 40° (*Fr* Cx. *Supp.* 1920, 41).

**Solubility.** 100 parts are liquefied by 10 of water, form a clear liquid with 30 to 40 of water, and are completely dissolved by 1300 of water. Also soluble  $3\frac{1}{2}$  in 1 of glycerin, 3 in 1 of chloroform (nearly), 1 in 2 of olive oil, 5 in 1 of ether, 6 in 1 of alcohol (90%),  $2\frac{1}{2}$  in 1 of benzene and 1 in about 20 of soft paraffin.

1% of phenol in liquid paraffin forms a saturated solution. More will dissolve warm but is thrown out again on cooling. It was thought that the addition of menthol might form a non-escharotic compound, and hence alleviate the effect of the phenol, but this is erroneous. A case turned on the subject some years ago,

in which a large proportion of phenol (plus menthol) had been prescribed as ear-drops

**Incompatibility.** A solution of lead subacetate gives a precipitate with phenol, but there is no change with the acetate. Other phenols, cresols, etc., do likewise, except pyrogallol. The precipitate may be prevented by adding a trace of acetic acid to the subacetate solution—G A. Medley, *Pharm J*, 11/1926, 149

The precipitate formed is apparently of the formula  $Pb(O C_6H_5)_2$ ,  $Pb(OH)(O_2C CH_3)$ —E A. Lum, *ibid*, 1/1929, 149, 251, J E. Driver, *ibid*, 251, see also E. Matthews, 297 and E H. Lane, 321

**Antidotes.** Give emetic (not always effectual). Empty stomach by stomach tube, using 2 oz of magnesium sulphate or sodium sulphate in 2 gallons of water. Give 1 oz of magnesium sulphate in 1 pint of water to be retained. Demulcents, such as white of egg, mucilaginous drinks, do not give alcohol, oils, fats or glycerin. Keep patient warm. Artificial respiration and oxygen inhalation if necessary. Strychnine,  $\frac{1}{4}$  gr, hypodermically. Saline infusion.

Case of phenol poisoning recovered after successive aspiration of stomach and gastric lavage with saline, diluted egg albumen and 50% alcohol respectively, caffeine and adrenaline given as stimulants, glucose and saline intravenously, 40 ml of 1% methylene blue solution intravenously. Suggested that this may have influenced favourable outcome—W M. Sheppe, *Milit Surg*, 1935, 76, 30

**Uses.** A powerful antiseptic, anti-putrefactive, caustic and, applied locally, anæsthetic. Internally for dyspepsia and flatulence, e.g., with rhubarb and nux vomica extract in capsule. Also, in enteric-coated pills, in typhoid fever and diarrhœa, and in erysipelas, puerperal fever, phthisis, bronchitis, pertussis, and for the gangrenous stage of pneumonia.

As a vaginal injection, 1 in 80 or more of water for leucorrhœa, uterine ulceration, erysipelas and cancer; cleanses, heals, disinfects and allays pain, and is suitable as a gargle. A 2% solution in alcohol is used for diphtheritic membrane. In acne the pustules may be treated by evacuating the contents and applying the smallest possible quantity of a mixture of phenol and camphor, equal parts. The same mixture has been applied to war wounds and to hypopyon ulcers.

Mosquitoes are kept away by 1% solution. It also relieves bites of same. 2% is effective for disinfecting instruments and the skin, and as an antiseptic for artificial dentures. A 1% spray is useful in acute coryza.

**ANTHRAX.** 1 to 2 ml of 5% phenol beneath and round the pustule effects complete and dramatic cure. Cheap and painless and all except severe cases treated as out-patients—G C. Dorling, *Brit med J*, 1/1932, 123.

Inject 2 to 3 ml of 5% phenol in 2 to 4 places around and into the base of the pustule, if very large 5 ml may be needed. Merely a simple dressing is then applied. If, on the following day, there are any signs of the pustule progressing, a further injection is made at that site, but often only one injection is required. Within 48 to 72 hours the pustule dries up and in 7 to 10 days the centre separates, but unless an excess of carbolic has been used the scar is usually quite small. Of 16 cases 2 died, and they were in an advanced stage—G C. Dorling, *Chinese med J*, 1935, 662.

**HÆMORRHOIDS** may be treated by interstitial injection of phenol in almond oil, see Carbolic Almond Oil, also in liquid extract of hamamelis—See Hamamelis.

**SMALL-POX** pustules have been touched with liquefied acid with good results.

**TETANUS** treated by intrathecal injections Phenol kills tetanus toxin in vitro. 1 in 400 solution employed—30 to 40 ml. for adults. 10 out of 14 cases recovered.—S. Suvansa, *Lancet*, i/1931, 1075.

**VARICOSE VEINS.** Injection of undiluted liquefied phenol 2 to 4 minims preferable to quinine-urethane, sodium salicylate, etc., which give rise to considerable pain and are dangerous in cases of idiosyncrasy. The carbolic acid is at once locked up in the clot, which forms immediately. 4 minims is sufficient to obliterate a large varicose saphenous vein. The injection is practically painless and the vein almost immediately hardens. Four to eight veins may be injected at a sitting. Veins do not become immunised to the acid.—P. P. Dalton, *Brit. med. J.*, ii/1928, 1037

**VOMITING.** Immediate and dramatic effect in a case of persistent and uncontrollable vomiting in a case of uræmia, following a 2-minim dose of phenol. Phenol is a gastric sedative of great value, and is of benefit in many cases of gastritis and, used with morphine, gives astonishing relief in inoperable carcinoma of the stomach.—J. C. Lyth, *Brit med J*, ii/1935, 903.

**Carbasus Phenolis (B.P.C.).** *Syn.* CARBOLIC GAUZE. Contains 1 to 3% of phenol when freshly prepared.

**Gossypium Carbolisatum.** *Syn.* PHENOL WOOL.

To prepare this, impregnate absorbent cotton 1 under pressure with 1 of an ethereal solution (5%) of phenol. Spread out and dry rapidly. **Linteum Phenolis** is also prepared.

**Cataplasma Phenolis (B.P.C.).** 2% in linseed poultice

**Collodium Carbolisatum (B.P.C.).** A jelly consisting of equal parts of phenol and simple collodion. A local anæsthetic for application to decayed teeth.

**Collut. Pot. c. Phenol. (N.I.F.)** Solution of potassium hydroxide 2 dr., liquefied phenol 2 dr., solution of bordeaux B 40 m., water to 8 oz. 1 tablespoonful in  $\frac{1}{2}$  pint of warm water.

**Gargarisma Phenolis (B.P.C.).** Glycerin of phenol 5% v/v in water. For foul breath and sore throat.

**Garg. Phenol. Co. (N.I.F.).** Liquefied phenol 2 dr., solution of potassium hydroxide 2 dr., trypan blue  $\frac{1}{2}$  gr., glycerin 1 oz., water to 8 oz. 1 tablespoonful to  $\frac{1}{2}$  pint of warm water

[P2] **Glycerinum Phenolis (B.P.).** *Syn.* GLYCERINUM ACIDI CARBOLICI.

**Dose.**—5 to 15 minims (0.3 to 1 ml.).

Phenol 16, glycerin 84. The preparation is *unnecessarily strong* for general local use. It is employed as a throat pigment and is applied to wounds and to ringworm. It has been used in acute middle ear catarrh with good result.

A solution of phenol in glycerin is almost non-caustic and only slightly toxic. **Caution (B.P.).**—Dilution with water renders it caustic. It may be diluted with glycerin.

**ITCHING OF ECZEMA.** Phenol 4 grains, glycerin 40 minims, alcohol 90% to 1 ounce is often useful, but may irritate.

**CARBUNCLES** are well treated by applying pledgets soaked in the glycerol. As soon as pus shows, the epithelium is turned back and the part may be later syringed out. Hygroscopic action of the glycerin prevents absorption.

[P2] **Gutt. Auribus Phenol. (N.I.F.).**

Glycerin of phenol 3 dr., glycerin 5 dr.

For earache, a few drops of solution of phenol in glycerin, slightly warmed, are invaluable. This strength is ample.

[P2] **Injectio Phenolis.** **Dose.**—5 to 20 minims (0.3 to 1.2 ml.). 2%.

This has been used for tetanus, erysipelas, and phlegmonous inflammations of the skin.—Whitla.

[P2] **Injectio Phenolis et Olei Amygdalse (C.X.H.).** Phenol 20 gr., menthol 1 gr., almond oil to 1 oz. For perivenous injection in hæmorrhoids, 5 ml. can be injected around each of not more than two separate hæmorrhoids at a time

[P2] **Carbolised Almond Oil.** Phenol 1, sterile almond oil to 20.

HÆMORRHOIDS well treated by injection of 1 to 2 ml. for each pile, under the mucous membrane, and injections continued at 5 to 7-day intervals until piles are of parchment-like hardness. Requires special instruments, skill, and experience.—A. S. Morley, *Lancet*, i/1928, 545. See also W. B. Gabriel, *Lancet*, i/1930, 162.

V. Meisen now adopts 5% phenol in almond oil.—*Lancet*, i/1931, 877.

W. S. Perrin uses phenol 1, glycerin 2 and water 2—usually a 5-minum dose. —*Lancet*, i/1929, 569. W. B. Gabriel uses 5% of phenol in almond oil—with usually 3-ml. dose—as also E. T. C. Milligan. Sir Charles Gordon Watson uses 15% phenol in glycerin and A. S. Morley 5% in oil.—*Brit. med. J.*, i/1931, 897.

If the vegetable oil be boiled for an hour and then filtered and the phenol added subsequently, the influenza-like symptoms which sometimes follow injection will not occur.—G. Sacks, *Brit. med. J.*, i/1933, 313.

COMPLETE RECTAL PROLAPSE satisfactorily treated by carbolised almond oil, but injections should be given deeply enough to reach the muscular coat, the aim being to inject all round the rectal wall: usually 2 to 3 ml is required, 4 or 5 injections being given at weekly intervals. Relapses are probable, but patients should be given the option of trying the injections before resorting to more drastic operations.—A. S. Morley, *Brit. med. J.*, ii/1934, 204.

[P2] **Sterules of Carbolised Almond Oil (Martindale, London)** contain 1 ml. of 5% solution.

[P2] **"50% P-O."**

Melted crystalline phenol 1 oz., warm almond oil 1 oz. and menthol 40 gr. This is the stock solution. [P2] The working solution (5% P-O) is 1 part of the 50% P-O with 9 parts of warm almond oil. 3 to 5 ml. of this injected high up above the piles produces sclerosis lasting many weeks.—W. B. Gabriel, *Practitioner*, i/1931, 115.

[P2] **Obturatin (Mayer's Formula).**

Zinc sulphate 1 dr., phenol cryst. 6 dr., glycerin 4 dr., Aq. Cinnamomi 1 oz., fluid extract of *Pinus Canadensis* (dark) 5 dr., redistilled water 2 oz. Dissolve the zinc sulphate in the cinnamon water; liquefy the phenol by heating, add the glycerin, shake and cool. Add the distilled water and the *Pinus Canadensis* and shake. Allow to stand for a week, shaking daily. Filter. The solution is muddy when cold but becomes clear on heating. Boil before injection. For the injection treatment of inguinal hernia inject  $\frac{1}{2}$  ml. first injection and 1 ml. subsequently (15 to 20 being the average at 4 to 7-day intervals). Insert needle vertically over site of internal ring till point is felt to pierce the aponeurosis. withdraw needle after every few drops to make sure the point is still outside any vessel. End-results compare favourably with operation. Patients not suitable for the treatment are those in which the hernia is not completely reducible or satisfactory fitting of a truss is impossible, active venereal disease or history of tuberculosis; in children, cases of hæmophilia.—St. G. B. Delisle Gray, *Brit. med. J.*, ii/1932, 13. "Obturatin" is not a proprietary—*Ibid.*, ii/1932, 385.

[P2] **Liquor Phenolis Alkalinus (B.P.C.).** *Syn.* SOLUTION OF SODIUM PHENATE.

Phenol 10% *w/v* with sodium hydroxide and water. Diluted with 20 to 30 parts of water it is used as a mouth-wash.

[P2] **Phenol Sodique (Fr. Cx.).**

Phenol 100 g., sodium hydroxide solution 20 g. (30% by weight), water to 1000 ml. The sodium hydroxide in this is insufficient to combine with the phenol. The *Fr. Cx.* preparation, in fact, contains about 8.6 g. per 100 ml. of free phenol, only 1.4 of the total 10 g. being in the combined condition.

[P2] **Liquor Potassii Phenatis Compositus (B.P.C.).** *Syn.* LIQUOR POTASSII CARBOLATIS COMPOSITUS.

A flavoured preparation containing 5% *v/v* of liquefied phenol in alkaline solution.



**[P2] Liquor Sodii Phenatis Compositus (B.P.C.)** *Syn* LIQUOR SODII CARBOLATIS COMPOSITUS, PHENOL SODA. A flavoured preparation containing 3% *w/v* of phenol as sodium phenate.

**[P2] Lotio Phenolis (B.P.C.).** *Syn* CARBOLIC ACID LOTION  
1 in 80, coloured pink.

Carboluric ochronosis due to use of 5% phenol lotion as dressing to leg ulcers over 35 years.—J L Berry, *Lancet*, ii/1931, 124

**[P2] Lotio Phenolis (R L O H)** *Syn* LOTIO ACIDI CARBOICI (R L O H)  
Liquefied phenol 24 m, sterilised water at 50° to 1 oz

**[D P1 81] Lotio Phenolis et Cocainæ.**

Phenol  $\frac{1}{2}$  dr, cocaine hydrochloride  $\frac{1}{2}$  dr, cherry laurel water 1 oz, rose water 3 oz For pruritus

In the later stage of treatment of chronic eczema a lotion containing phenol, liquor Picis Carbonis, glycerin and spirit may be used as a stimulant to growth of healthier epidermis

**[P2] Smith's Sterilising Solution.** Phenol 20, borax 5, glycerin 200, peppermint water 30, water to 1500 parts

**[P2] Ravogli's Liniment.** Phenol 1, glycerin 2, alcohol 90% 16, rose water to 32. In skin affections.

**[P2] Oleum Carbolisatum (B.P.C.)** *Syn.* CARBOLIC OIL  
1 in 20, in arachis oil For burns and scalds.

Scarlet fever has been treated by applying 5% phenol in olive oil all over the body, except the face, twice daily, followed by a warm bath at night.

**[P2] Oleum Lubricans (B.P.C.)** *Syn* LUND'S OIL, CATHETER OIL.

Phenol 5% *w/v* in castor oil and arachis oil. For oiling catheters  
Carbolised catheter oil has no value —O S Gibbs, *Brit med J*, i/1931, 581

**Surgical Lubricant** for catheters, etc

Starch 4, glycerin 35, add water  $8\frac{1}{2}$ , heat to boiling, remove from flame and add boric acid in powder 2 $\frac{1}{2}$ , warm to dissolve, and when nearly cold add phenol 1 The lubricant is non-greasy and does not attack rubber goods It can be removed by water It will not attack metal instruments if left in contact for a short time, but is not intended as a coating to store them in—for this, soft paraffin or liquid paraffin is best

**[P1] Catheter Lubricant (Meltzer's Formula).**

Triturate tragacanth 3 with glycerin 20, add water 100, and sterilise, then add mercury oxycyanide 0.25

*See also* Pasta Tragacanthæ Composita, p. 904

**Pastillus Phenolis** (Glycogelatin Basis)

Contains  $\frac{1}{2}$  grain (0.03 g) phenol Antiseptic and stimulant For ulcers in the mouth or throat and for purifying the breath

**[P2] Phenol cum Camphora (B.P.C.)** *Syn* CARBOLIC CAMPHOR. Phenol 25% *w/w* with camphor

Is not miscible with water or glycerin Antiseptic and local anæsthetic, serviceable in toothache.

Ulcers produced by X-ray burns have been treated locally by a mixture of equal parts of phenol and camphor

**Caution.** Not intended for extensive use. It is not suited for applying all over the face Accidents have occurred

**[P1] Phenol Iodisatum (B.P.C.)** *Syn.* IODISED CARBOLIC ACID, PIGMENTUM IODI CARBOLICUM.

Iodine 10% *w/v* in liquefied phenol.

[P1] **Acidum Carbolicum Liquefactum et Iodum** (C H W.) has iodine 1, liquefied phenol 4

For intrauterine medication on cotton wool. Chronic discharging sinuses have been treated by 5 minutes' application of iodised phenol, also inoperable uterine carcinoma after curetting Useful also for ringworm of the scalp

CHRONIC HYDROCELE of the tunica vaginalis well treated by injection into the cavity of iodised phenol (4 parts of iodine to 2 parts of phenol), withdraw all fluid from the sac and, with the needle *in situ*, inject iodised phenol 3 minims for every ounce of fluid withdrawn Massage scrotum for 5 minutes and apply collodion dressing Patient rests in bed for 24 hours with scrotum supported on a pillow Not more than 5 ml should be given at one sitting Better to commence with 2 ml—Morton Whitley, *Brit med J*, 11/1932, 241.

Carefully distinguish from —

**Dilute Iodised Phenol Injection.** Lugol's solution 2.5, phenol 1, boiling water to 200 Much weaker than the preceding Is used as a pigment in diphtheria, or as a gargle or inhalation Is useful also as a nasal douche in ozæna and for intrauterine injection

[P1] **Phenol Liquefactum** (B P) *Syn* ACIDUM CARBOLICUM LIQUEFACTUM

*Dose* —1 to 3 minims (0.06 to 0.2 ml) *U S P XI* average dose 1 minim

Contains 80% *w/w* of phenol Sp gr about 1.063 The congealing point of liquefied phenol of this strength is 3°, and the trouble experienced with the B P '14 preparation (87% *w/w* of phenol) from crystallisation in cold weather is thus obviated If cooled below the congealing point it should be completely melted before use *P Belg IV* has phenol 10, water 1, *P Dan* phenol 9, water 1, *P. Helv V* phenol 85, water 15

[P1] **Phenol Liquefactum** (L S P XI)

*Average dose* —1 minim (0.06 ml) Prepared by liquefying phenol in its unstoppered container by heating in a water bath and adding 1 part by weight of water to 9 parts by weight of phenol

[P2] **Phenosalyl.**

Phenol 60 g, lactic acid and salicylic acid, of each 5 g, borax 8 g, menthol, thymol and eucalyptol, of each 0.1 g, glycerin 20 g, water to 1000 ml—*Formulaire des Pharmaciens Français*, 1933 *P Dan* is similar. 0.2 to 0.4% in conjunctivitis and 1% in eczema

[P2] **Pigmentum Antisepticum.**

Glycerin of phenol 1 oz, quinine hydrochloride 30 gr Forms a useful pigment for the nasal passages in hay fever.

[P2] **Pigmentum Carbol-Fuchsin** (St T H) Saturated solution of basic fuchsin 10 ml, phenol 5 g, boric acid 1 g, resorcinol 10 g, water 100 ml Dissolve the phenol in the water, add the fuchsin solution, filter, add the boric acid, allow to stand for 2 hours and add the resorcinol To be stored in the dark in a stoppered amber-coloured bottle

**Pilula Phenolis.** *Syn* PILULA ACIDI CARBOLICI

Phenol 2, powdered liquorice 1, powdered althæa 1. In grains for 1 pill, in grammes for 15 pills

**Resina Acidi Carbolici** (R D H)

Colophony 4, phenol 4, chloroform 3 Dissolve and filter

This is used as an obtundent and a temporary antiseptic filling *Method* — Syringe out all food from the cavity and remove as much decay as possible Apply on a wool pledget to relieve toothache

**Resina Carbolisata** (B P C) Phenol 1, mastic 1, colophony 2, chloroform 1.

[P2] **Solutio Phenoli** (I A) contains 2% of phenol. *Aqua Phenolata* (*P Helv I'*) and *Aqua Carbolisata* (*P Tap*) are this strength

[P2] **Solutio Phenolis et Glycerini** (*St. T. H.*). Phenol 48 gr., glycerin 2 dr., water to 4 dr. *Dose* —2 to 5 minims paravenously For hæmorrhoids.

[P2] **Preservative Solution** for anatomical specimens

Phenol 1, glycerin 4, methylated spirit 5.

**Stupa Phenolis** (*B.P.C.*). *Syn.* CARBOLISED TOW. Contains 5% of phenol when freshly prepared.

[P2] **Suppositorium Phenolis** (*B.P.*). *Syn.* SUPPOSITORIUM ACIDI CARBOLICI.

Unless otherwise stated, contains 1 grain (0.06 g.) of phenol in a 15-grain suppository. May be made with  $\frac{1}{2}$  grain of white beeswax and oil of theobroma *q.s.*

[P2] **Trochiscus Phenolis** (*B.P.*). *Syn.* TROCHISCUS ACIDI CARBOLICI. Contains  $\frac{1}{2}$  grain (0.03 g.) with sugar basis. For sores in mouth and throat.

The loss of phenol from the lozenges is considerable under all ordinary conditions of storage, and may average 1 mg per month. The strength is usually under 0.03 g. per lozenge —C A Hill and A. D Powell, *Quart J Pharm.*, 1934, 535.

**Unguentum Phenolis** (*B.P.*). *Syn.* UNGUENTUM ACIDI CARBOLICI. Phenol 3% in a basis of white beeswax, lard, hard and soft paraffins. Lard is used owing to the small solubility of phenol in paraffins. For ulcers and parasitic skin diseases.

Water-miscible bases should be used for all ointments, such as ointment of phenol, intended for use as bactericides —E. Gershenfeld and R E Miller, *Amer. J Pharm.*, 1933, 194

**Unguentum Phenolis** (*U.S.P. XI*). Phenol 2, yellow wax 5, petrolatum 93. The yellow wax and phenol are melted on a water-bath, the petrolatum added and the mixture stirred until it congeals. It is required to contain from 1.8 to 2.2% of  $C_{12}H_{25}OH$ .

**Unguentum Phenolis Compositum** (*B.P.C.*). Phenol about 18%, with sulphur, olive oil, beeswax and strong ointment of mercuric nitrate.

**BOILS.** Boils of a subacute type may respond favourably to the following ointment: phenol 1%, camphor 3%, salicylic acid 2%, lanoline-vaseline  $\frac{1}{2}$  oz. A thick layer of the ointment on a piece of lint is laid on the boil and changed as often as required. Soothing, antiseptic, and hastens separation of the slough. —John Fraser, *Practitioner*, 1/1936, 359.

[D-P1-81] **Unguentum Phenolis cum Cocaina.**

Liquefied phenol 20 m., cocaine hydrochloride 10 gr., white soft paraffin 1 oz.

[P2] **Unguentum Phenolis cum Hydrargyri Perchlorido.**

Liquefied phenol  $\frac{1}{2}$  dr., mercuric chloride 2 gr., olive oil 2 dr., zinc ointment to 1 oz.

Both the above are used for pruritus.

**Unguentum Phenolis cum Menthole.**

Phenol 2, menthol 1, cold cream 100. For eczema with much itching.

**Vapor Phenolis.**

20 drops of liquefied phenol in a pint of water at 60°. Inhaled or as a spray in pertussis and for throat ulcers. It lessens and disinfects the expectoration in bronchitis and gangrenous lung.

[P1] **Vapor Phenolis Compositus** (*B.P.C.*). Creosote 1% *v/v*, oils of eucalyptus and Siberian fir 2% *v/v*, in liquefied phenol.

**Smelling Salts, Carbolic.**

Phenol 24, ammonium carbonate 16, strong solution of ammonia 44, oil of lavender  $1\frac{1}{2}$ , camphor 8, pine sawdust (sifted) *q.s.* For coryza, hay fever, influenza, etc.

**Anti-Catarrhal Salts.**

Phenol 1, eucalyptus oil 1, oil of pumilio pine  $\frac{1}{2}$ , strong solution of iodine  $\frac{1}{2}$ , camphor 1, ammoniated alcohol 2, pine sawdust 2 or *q.s.*

[P1] **Anusan Suppositories** (*Allen & Hanburys, London*) contain phenol, adrenaline, zinc oxide, benzocaine and Peru balsam in a lanolin base. **Anusan Ointment** contains the first three ingredients in a lanolin base. For hæmorrhoids, etc.

[P2] **Emollientine** (*Parke, Davis, London*). Ointment containing phenol 4½ gr. and mercuric chloride  $\frac{1}{2}$  gr per ounce, with lead oxide, zinc sulphocarbonate, etc. Beneficial in eczema, hæmorrhoids, ulcers, etc.

**Inhalone** (*Parke, Davis, London*). Ointment containing phenol 1½ gr. per oz, menthol and eucalyptol in soft paraffin. Relieves congestion of nasal passages.

**Phenofax** (*Burroughs Wellcome, London*). Phenol ointment containing 3% of phenol. In pruritus and irritant skin conditions and as a stimulating dressing for small wounds.

**Acidum Phenolsulphonicum.**  $C_6H_4(OH)SO_3H = 174.1$ .

*Syn.* SULPHOCARBOLIC ACID, SOZOLIC ACID.

Prepared by the action of strong sulphuric acid on phenol. The *para*-acid is produced in the warm, the *ortho*- when working in the cold; crystallises with difficulty, dissolves readily in water, alcohol, and glycerin, and is a strong antiseptic and disinfectant.

In gingivitis and pyorrhœa a 3% solution is useful, reduces swelling and arrests flow of pus. A 33% solution has been sold as **Aseptol**.

**Cupri Phenolsulphonas.** *Syn.* CUPRI SULPHOCARBOLAS, CUPRI ASEPTOL.  $(C_6H_4(OH)SO_3)_2Cu, 6H_2O = 517.8$

In light green crystals, soluble in water, a useful hæmostatic or antiseptic lotion or astringent injection,  $\frac{1}{2}$  to 1½%.

CHOLERA has been treated with small doses ( $\frac{1}{2}$  gr. per hour).

**Sodii Phenolsulphonas (B.P.C.).** *Syn.* SODII SULPHOCARBOLAS  $C_6H_4(OH)SO_3ONa, 2H_2O = 232.1$ .

*Dose*—5 to 15 grains (0.3 to 1 g.).

In white rhombic crystals, slightly efflorescent in dry air.

**Soluble** 1 in 6 of water, 1 in 150 of alcohol 90%, 1 in 5½ of glycerin.

**Uses.** In dilatation of the stomach due to flatulence and fermentation. For flatulence, the dyspepsia of phthisis and in tonsillitis 5 to 10 grains every 2 hours have been given.

Carbolic saturation to prevent the growth of *streptococci* in the circulating fluids. 20 to 25 grains of sodium phenolsulphonate needed for an adult every 2 hours. Treatment is stopped immediately there are any signs of phenol poisoning—T. S. Wilson, *Brit. med. J.*, ii/1927, 57.

**Mist. Sod. Sulphocarb. (N.I.F.)** Sodium phenolsulphonate 5 gr., potassium bicarbonate 10 gr., water to  $\frac{1}{2}$  oz.

**Zinci Phenolsulphonas (B.P.C.).**

$(C_6H_4(OH)SO_3)_2Zn, 8H_2O = 555.7$  *Syn.* ZINCI SULPHOCARBOLAS.

Colourless rectangular crystals. Soluble 1 in 2 of water, 1 in 2½ of alcohol 90%.

In gonorrhœa and leucorrhœa; 2 or 3 gr. per oz. for injection. Also as a nose or throat spray (5 gr. per oz.).

**Tribromophenol.**  $C_6H_2Br_3 \cdot OH = 330.7$ . *Syn.* BROMOL.

*Dose.*— $\frac{1}{2}$  to 2 grains (0.03 to 0.12 g.) in pill.

Manufactured by adding bromine 120, in small portions, to phenol 53, dissolved in water, *q.s.*, with continuous stirring and recrystallising the product from spirit.

In long silky needles, nearly insoluble in water, soluble 1 in 3 of

alcohol 90%, 1 in 1 of ether, 1 in 3 of chloroform and glycerin, also soluble in fats and oils M p 85°. Used alone is strongly antiseptic. ointment (10%), oily solution (1 in 30). Is not dissolved by gastric juice, and is used as an intestinal disinfectant and in typhoid, also in minute doses for cholera infantum

**Bismuthi Tribromphenas** (*B P C*, *P Helv V*, *P G VI*, *P Jap. IV*, *P. Ned V*). *Syn and Prop Name* BROMPHENOL BISMUTH, BROMPHENOBIS, BISMUTUM TRIBROMOPHENYLICUM (*P Ital V*), XEROFORM (*Bayer Products, London*) No formula is given in *B P C* *P. Helv. V* gives  $(C_6H_2Br_3O)BiOH, Bi_2O_3$ .

*Dose*.—5 to 15 grains (0.3 to 1 g.)

A yellowish insoluble powder, with faint odour and taste, containing 40.5 to 49.5% of Bi. An intestinal antiseptic, *e g*, for cholera

**Trichlorphenol.**  $C_6H_2Cl_3OH$  *Syn* TRICHLORPHENIC ACID

White crystals with pungent taste, soluble 1 in 1 of alcohol, 2 in 1 of ether, 1 in 9 of glycerin, also in fixed and volatile oils

Ointment and solution 10% strength are used as antiseptics

**Para-Monochlorphenol.**  $C_6H_4ClOH$  = 128.5 Crystalline needles soluble in alcohol and ether, but not in water to any extent M p 37°, b p 217° Liquid *para*-monochlorphenol is practically identical and is used similarly The *ortho*- body boils at 176° and the *meta*- melts at 28.5° and boils at 212°

A powerful antiseptic used in treatment of lupus, phthisis, keratitis, iritis, and is also employed in dental work as an analgesic A paste for filling is made with cobalt and tropacocaine hydrochloride equal parts, with enough monochlorphenol and zinc oxide to produce a paste The unpleasant taste may be moderated by menthol.

5 to 10% in glycerin has also been used for laryngeal catarrh Inhalations 1 to 4%

**Unguentum para-Monochlorphenolis.**

*para*-Monochlorphenol 1, 2 or 5, soft paraffin 50, hydrous wool fat 50 Chulblains are well treated with this and with solution of *p*-monochlorphenol To cover the odour lavender oil 5% is useful

**Tri-iodophenol,**  $C_6H_2I_3OH$ , has been used for making lotions and gargles

**Bismuth Tri-iodophenol.** *Syn* NEOFORM Yellowish powder insoluble in water Has antiseptic properties

**Dimol** (*Dimol Laboratories, London, Sangers, London*) Dimethyl-methoxyphenol,  $C_6H_3(CH_3)_2(OCH_3)OH$  = 152.1, in combination with tri- and tetramethylphenols, in tablet form Has R W coefficient of not less than 42 and is voided in the faeces unchanged *Dose*—In 1-grain tablets, 2 to 4 with water after each meal, also in syrup, strength 0.3 gr per drachm It has been well spoken of in dysentery, colitis and intestinal toxæmias generally

Chronic dysentery, sprue, mucous colitis, intestinal worms, auto-intoxication, etc., treated by colonic lavage, using a solution of 1 to 4 oz of Dimol powder in 8 gallons of hypertonic saline (4 oz of powder = 1.4 gr per oz) with good result. An investigation by Cuthbert Dukes showed marked effect on the effluent At 15 minutes there were 10 organisms and no *B coli* per ml against a control showing more than 200 bacteria and 800 *B coli*—W Kerr Russell, *Brit J. phys Med*, May, 1931

**THE ACTION OF CERTAIN ALLEGED INTestinal ANTISEPTICS** Neither Dimol, Kerol, Izal, or Yatren were found to exert any appreciable effect on the total numbers of living aerobic organisms in the faeces when administered by mouth in adequate doses The first three were found to exert on faeces *in vitro* an antiseptic action much greater for coliform bacilli than for streptococci, the concentration of the drugs being considerably higher than in the intestinal tract, which presumably follows their administration by the mouth Yatren had no evident action whatever in any dilution employed "Specific and detailed evidence as to the alleged action of these drugs should be published in support of the claims constantly made for them"—L P Garrod, *Brit med J*, 1/1926, 369.

Garrod's conclusions, as far as Dimol is concerned, according to the makers of Dimol, are *contra* to clinical evidence. Method of enumerating bacteria in faeces not accurate to within 100%. Whereas *B. coli* normally present are not affected, the causal infective organisms are destroyed by the drug. *B. coli* count alone thought of no value.—*Brit med J*, 1/1926, 505

[P] 81 [84] **Dinitrophenol.**  $C_6H_3(NO_2)_2OH = 184.0$  Syn  
2 4-DINITROPHENOL

[P1], [81] and [84] "*Dinitroresols; dinitronaphthols, dinitrophenols, dinitrothymols*"

[83] "*Dinitrophenols—in substances not being preparations for the treatment of human ailments*"

Yellow crystals sparingly soluble in cold water, readily soluble in hot water and in ether, benzene or chloroform. Given internally it raises the metabolic rate, and has been given (mainly in America), in doses of about 5 gr per day, for the reduction of obesity. Numerous cases of poisoning have occurred, agranulocytosis, cataract and other lesions being produced, and its use is now regarded as inadvisable.

**Antidotes.** Empty stomach by stomach tube, using 2 gallons of 5% sodium bicarbonate solution, or 1 in 2000 potassium permanganate. Oxygen inhalations. Place patient in an ice pack to bring down temperature. Dextrose or dextrose in saline intravenously.

Treatment of acute dinitrophenol poisoning.—Tainter, *J Amer med Ass*, 1/1935, 1071.

Case of poisoning by dinitrophenol, with recovery.—Geiger, *J Amer med Ass*, 1/1935, 915.

Numerous cases of rapidly developing cataract following the use of dinitrophenol in the treatment of obesity. Blurring of vision occurs after a time, which rapidly goes on to blindness from complete lens opacity. The cataract may develop some time after the patient has discontinued the treatment.—W. D. Horner, R. B. Jones, and W. W. Boardman, *J Amer med Ass*, 11/1935, 108, *ibid*, 793.

Surprisingly rapid improvement following the use of ascorbic acid in this condition (also gratifying results in senile cataract).—F. M. Josephson, *Science*, 1935, 82, 222.

Dinitrophenol is unpredictably toxic, except that persons with chronic rheumatism, tuberculosis, alcoholism, renal disorders and hepatic disease seem to have a lessened resistance. There is no known specific chemical antidote. In view of the rapidly increasing number of untoward effects of this drug, such as peripheral neuritis, cataracts, anaemia, thrombocytopenia and purpura, physicians should make every effort to discourage its use.—S. W. Imerman and C. P. Imerman, *J Amer med Ass*, 1/1936, 1087.

A powerful and rapidly acting stimulant to oxidative metabolism which does not upset pulse rate or blood pressure. The excess metabolism, which subsides when the drug is withdrawn, is conducted largely at the expense of fat. In doses of 3 mg per kilo, it may increase metabolism to as much as 50% over its original level. Serious toxic effects have been recorded and uncomfortable sensations of excessive warmth, sweating and lethargy may necessitate a lower dose. Below 3 mg per kilo, however, it is likely to be singularly ineffective in lowering excess body weight, and even in maximum therapeutic dosage it does not compare as a weight reducer with thyroid or dietetic restriction. It is no substitute for thyroid in myxoedematous states.—D. M. Dunlop, *Brit med J*, 1/1934, 527. See also *ibid*, 539.

**EFFECT ON METABOLISM.**—The effects of dinitrophenol on the energy exchange and metabolism of three patients were studied under controlled conditions, using a fixed diet of low caloric value and minimal protein content. Quantitative urinary, fecal and blood metabolite determinations were made throughout. The energy exchange was calculated from measurements of the respiratory quotient

and nitrogen excretion. A week or more was used for control observations and then 0.3 or 0.4 g. of dinitrophenol was given daily for from one to two weeks. This period of medication was followed by a second or after-control period of about one week. These results showed that moderate dosage of dinitrophenol caused marked stimulation of metabolism, the extra energy being derived mainly from the complete combustion of fat without affecting significantly the protein or nitrogenous constituents of the body.—M. L. Tainter, W. C. Cutting and E. Hines, *J. Pharmacol.*, 1935, 55, 326.

[P1-81-84] **Dekrysil** (*British Colloids, London*). Capsules containing 0.05 g. of 4 : 6-dinitro-*o*-cresol. *Dose*.—0.0005 to 0.001 g. per kg. body weight. Given as a metabolic accelerator for the treatment of obesity.

Inquest on a young dancer who sought to reduce her weight by treatment which included Dekrysil. Death was found due to nitrophenol poisoning, traces of nitrophenol being found in the intestines and stomach. She had possibly taken 17 capsules in 3 days. All concerned were exculpated except the patient: the chemist had cautioned her to take them only under doctor's orders; the manufacturer's label on the bottle was a clear warning to the same effect, and the medical practitioner had given her careful directions, which she had disregarded.—*Lancet*, 1/1934, 652.

It is possible with dinitro-*o*-cresol to maintain the metabolic rate at a figure some 30 to 50% above normal without the appearance of any discomfort or toxic symptoms and, provided diet is not grossly in excess of requirements, weight will be lost and the intake may be adjusted so that steady loss of weight results. Dinitro-*o*-cresol is in the region of 5 times as potent as the dinitrophenol compound.—E. C. Dodds and J. D. Robertson, *Lancet*, 11/1933, 1139.

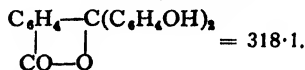
Since it is possible to control obesity even of frankly endocrine origin by means of dieting alone it is clearly undesirable to use a drug which is poisonous in doses only a little above those which are effective.—A. H. Douthwaite, *Brit. med. J.*, 1/1934, 701.

The danger with this type of compound lies not in its effects on the liver and kidneys, but on overstimulation of the metabolism from overdosage. The real risk arises from indiscriminate use of the drug. Provided a careful watch is kept on the patient and the basal metabolic rate is measured frequently there is no danger in their use. Animal experiments show that the toxicity of these drugs is solely due to their power of raising the metabolism to such an extent that death supervenes.—E. C. Dodds and J. D. Robertson, *Lancet*, 1/1935, 1241.

Adequate supervision is only really effective in hospital or nursing-home. It is doubtful if patients suffering from obesity and carrying on their ordinary avocations can be trusted to obey implicitly the injunctions of their medical advisers as regards dosage. It is here that the danger comes.—Sir W. H. Willcox, *ibid.*, 1413.

## PHENOLPHTHALEINUM

*B.P.*, *U.S.P. XI*, *P. Ital. V*, *P.G. VI*, *P. Belg. IV*, *F.E. VIII*,  
*P. Dan.*, *P. Helv. V*.



*Syn. and Prop. Name.* DIHYDROXYPHTHALOPHENONE, LAXOIN  
(*Oppenheimer, London*).

*Dose*.—1 to 5 grains (0.06 to 0.3 g.). Larger doses are used.  
*U.S.P. XI* average dose 1 grain.

A white crystalline powder, made by interaction of phenol and phthalic anhydride. *M.p.* (*B.P. Add.*) not below 258°; commercial samples may melt at temperatures up to 260°. Soluble 1 in 10 of alcohol 90%, also soluble in ether; almost insoluble in water.

*Uses.* As a purgative. Ordinarily  $\frac{1}{2}$  to 3 grains is sufficient, but patients confined to bed require from 3 to 10 grains. Does not

irritate the kidneys. It is satisfactory for prompt action, as in jaundice. It is more active than cascara and less griping, and has been found ideal in intestinal toxæmia.

Skin eruptions from phenolphthalein in U S A — *Brit. med. J. Epit.*, 1/1922, 81; *Prescriber*, 1922, 182, 246, *Brit. med. J. Epit.*, 1/1923, 81; *Clin. J.*, Dec., 1923, 611.

Capable of destroying red blood corpuscles and inducing toxic degeneration of the kidneys; cases cited — *Per Prescriber*, 1923, 15.

**Tabellæ Phenolphthaleini (B.P.C.)** contain 2 gr. (0.12 g.) in chocolate basis.

[P1] **Tabellæ Phenolphthaleini Compositæ (B.P.C.)**.

*Dose*.—1 to 3 tablets.

Phenolphthalein 1 gr., strychnine hydrochloride  $\frac{1}{100}$  gr., dry extract of belladonna  $\frac{1}{100}$  gr. A useful combination.

**Aperitol (Riedel-de Haen, Old Strand Chemical Co., London)**. 150 Valerianic ester of phenolphthalein and acetic acid ester of phenolphthalein, equal parts, in tablets containing 0.2 g. Aperient.

**Isolax (Richter, London)**. Diphenolisatin in tablets containing 0.005 g.

*Dose* — 1 or 2 tablets nightly. Aperient.

**Purgen (Kirby, London)**. Tablets containing phenolphthalein. Supplied as infant ( $\frac{1}{4}$  gr.), adult ( $1\frac{1}{2}$  gr.) and strong ( $7\frac{1}{2}$  gr.).

**Eosin** (Colour Index No. 768) is the sodium or potassium salt of tetrabromofluorescein. A reddish-brown powder soluble in water giving a red solution with green fluorescence. Ethyl eosin or spirit-soluble eosin (Colour Index No. 770) is the potassium salt of dibromo-dinitrofluorescein.

**Fluorescein**.  $C_{20}H_{12}O_5$  = 332.1. *Syn.* TETRAOXYPHTHALOPHENONE ANHYDRIDE, RESORCIN-PHTHALEIN ANHYDRIDE.

In yellowish-red powder, sparingly soluble in water, more so in presence of an alkali, e.g. sodium hydroxide, forming soluble fluorescein showing a green fluorescence.

**Fluoresceinum Solubile (B.P., U.S.P. XI)**  $C_{20}H_{10}O_5Na_2$  = 376.1. *Syn.* SODIUM FLUORESCIN, URANIN, OBITURIN.

Red crystalline powder, forming a red solution with intense greenish-yellow fluorescence which disappears on acidifying.

**Soluble** 1 in 1 of water, 1 in 5 of alcohol 90%.

**Uses.** The solution is used for detecting corneal lesions, e.g., when due to a minute foreign particle in the eye. Portions of the cornea not covered by epithelium are stained green. Has been employed by injection as a proof of death. If life is extinct there is no reaction; if death is only apparent, the integument and the eyes turn green in a few minutes.

**Activated (irradiated) Fluorescein in Treatment of Cancer.**

Slightly alkaline (not neutral) solution of soluble fluorescein sprayed or painted widely over the surface of the growth, followed by radium or X-ray irradiation of moderate penetration.

**ORAL USE.** Capsules of soluble fluorescein 1 to 3 g. (in 2 capsules) half an hour before treatment, or as a "swallow"—soluble fluorescein 5, sodium bicarbonate 3, glycerin 2, water to 100—for growths in pharynx etc., when it is impossible to spray (actually 1 drachm has been given in error for 1 g. without unpleasant symptoms). Feeling of sickness in some cases. It is excreted by the kidneys.

**PAINT.** Soluble fluorescein 2.5, sodium bicarbonate 3, glycerin 2, in water 100.



**INTRAVENOUS INJECTION.** For lung cases. Soluble fluorescein 5, sodium bicarbonate 3, in normal saline 100. Inject 20 ml. slowly, e.g., in 3 minutes. Treat immediately after injection

**NODULE INJECTION.**—Same as for paint.

**BLADDER INJECTION.**—Soluble fluorescein 2.5, potassium fluorescein 2.5, sodium bicarbonate 3, in normal saline 100. Leave for 10 minutes and then remove, leaving about 4 oz.

**ENEMA.**—Same as for bladder injection. Decant as much as possible.

Too strong concentration of fluorescein may cause X-ray erythema

120 cases treated at Royal Northern Hospital between 1927 and Nov., 1930—33 died and apparently 23 recovered (alive and well Nov., 1930). Other hospitals and private reports in addition. Allied dyes also investigated.—S. Monckton Copeman, *Brit. med. J.*, 1/1931, 658

See also *Franco-Brit. med. Review*, Oct., 1930, *J. State Med.*, Vol. XXXVI, No. 11, p. 642, Claude Goulesbrough, *Brit. med. J.*, 1/1931, 767

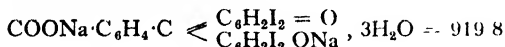
The external application causes no pain, and there are no unpleasant symptoms from the internal use, except yellow coloration of the skin, which disappears.—S. Monckton Copeman, *Brit. med. J.*, 11/1928, 223

Rapidly growing, i.e., more malignant, growths responded particularly. In breast cancers, enlarged glands in the axilla disappeared under fluorescein *per os*, although not themselves directly activated. In superficial secondary growths, e.g., recurrent nodules on or near the scar of an operation wound, good results were obtained by injecting with a needle a few drops of fluorescein solution into the substance of the nodule prior to irradiation. Treated in this way, secondary nodules, even of considerable size, may disappear with unexpected rapidity. Cases previously regarded as inoperable were, in certain instances, after activated fluorescein, found, at a comparatively early stage, to have undergone such changes as to render them amenable to surgical intervention with satisfactory results.—S. M. Copeman, Frank Coke and C. Goulesbrough, *Brit. med. J.*, 11/1929, 233

Criticism.—J. H. Douglas-Webster, *Brit. med. J.*, 11/1929, 367, 983, S. M. Copeman, *ibid.*, 929.

**Guttæ Fluoresceinæ (B.P.C.)** *Syn.* LIQUOR FLUORESCINÆ  
Soluble fluorescein 2% w/v

### **Iodophthaleinum (B.P.).**



*Syn. and Prop. Names* SOLUBLE IODOPHTHALEINUM (*U.S.P. XI*), SODIUM TETRAIODOPHENOLPHTHALEIN, IODO-RAY (*Martindale, London*), IODEIKON (*Mallinckrodt, St. Louis*), IOD-TEIRAGNOSI (*Merck, Darmstadt, Martindale, London*), OPACIN (*Pharmaceutical Specialties (May & Baker) Ltd, London*), STIPOLAC (*Burroughs Wellcome, London*)

**Dose.**— $\frac{1}{2}$  to  $\frac{1}{2}$  grain per pound body weight up to 75 grains (0.04 to 0.06 g. per kilogramme body weight up to 5 grammes). By intravenous injection, up to 45 grains (3 g.). *U.S.P. XI* average doses, oral 8 grains, intravenous 5 grains, per 10 kg. body weight.

A blue-coloured powder, somewhat hygroscopic, with a saline astringent taste. An aqueous solution may throw out on standing, owing to absorption of carbon dioxide and deposition of the acidic

body. It yields not less than 85% of the cream-coloured tetraiodo-phenolphthalein on precipitation with hydrochloric acid, the separated precipitate containing 61 to 62% of I

**Soluble** 1 in 7 of water; slightly soluble in alcohol 90%

**Toxicity.** An investigation by the Pharmacopœia Commission on 7 commercial samples showed little variation—0.37 mg per g weight of mouse for the least and 0.27 mg per g for the most toxic sample. The conclusion was that the compound from makers of good repute should show no important divergence of toxicity.—J Barba-Gose, *Quart J Pharm*, 1929, 396, *Lancet*, 1/1930, 522

**Uses.** It has been advocated as the most suitable of numerous chemicals which, following intravenous or oral administration, are excreted by the liver into the gall-bladder, rendering it opaque to X-rays (cholecystography)

#### **Oral Administration.**

The patient takes a fat-free evening meal, during which the iodophthalein may be given at intervals in capsules, preferably enteric-coated, or the requisite dose may be given in water some 2 hours later. No further food must be taken before the radiographic examination takes place. This may be at 10 a.m. and 1 p.m. the following day. Various other techniques are in use. Some authorities (*vide infra*) recommend fat (e.g., castor oil) when the drug is taken.

#### **Intravenous Administration.**

The usual dose is about 3 to 3.5 g in 30 to 50 ml of water. This is administered in two portions, with an interval of 30 minutes between each, the injection being made very slowly with the patient fasting, a light diet having been taken the previous day. Photographs may be taken after 3, 5 and 7 hours. A meal rich in fats is taken when the gall-bladder is outlined, and a further photograph is taken an hour later.

Intravenous administration requires care. The solution should be freshly prepared with sterile water, the drug itself should be carefully stored in order to avoid decomposition, and special care must be taken to avoid extravasation of the solution. The oral route is generally preferred in this country.

#### **Oral Administration in One Dose.**

This is the acidic form of the compound and may be prepared by admixture with 4.25% of citric acid. The dose is therefore a suspension of the white acid body which reverts to the blue soluble sodium salt in the intestinal canal.

Similar preparations are **Opacol** (*Pharmaceutical Specialties (May & Baker) Ltd, London*), and **Shadocol** (*Davies, Rose, Boston, Mass, Kodak Ltd, London*).

A correct diagnosis obtained in 95% of 467 patients.—E. V. Graham and co-workers, *J Amer med Ass.*, 11/1925, 953

In the majority of cases the gall-bladder can be seen clearly after oral use, which produces less frequent and less severe toxic symptoms.—A. F. Hurst, *Brit med. J.*, 11/1925, 1151

Diagnosis, treatment and prevention of gall-stones.—A. F. Hurst, *Brit med J.*, 11/1926, 677, *Lancet*, 1/1926, 966

Oral method employed almost exclusively at Middlesex Hospital. Variations in the strength of gastric and pancreatic juices cause trouble in perfecting a capsule coating. Possibility of local damage due to extravasation, a serious

drawback to intravenous use. *Technique*.—The patient is prepared as for an ordinary skiagram of the gall-bladder. An ounce of castor oil is given one night and  $\frac{1}{2}$  ounce the next. Light breakfast and a very light lunch are permitted on the following day, and an ordinary skiagram of the gall-bladder is taken in the afternoon. Tea and bread and butter are permitted on the same day and another small meal at 12 p.m., during which the drug is swallowed in the form of capsules. The dose given is 5 g. (4 g. if the patient weighs under 100 lb.), administered in  $\frac{1}{2}$  g. capsules. A cup of tea only is given on the following morning and X-ray examinations at 10 a.m., 2.30 p.m. and 4.30 p.m.—T. Izod Bennett and co-workers, *Lancet*, ii/1926, 20; *Brit. med. J.*, ii/1926, 195, 681.

Oral use is quite accurate enough for routine. Ill-effects insufficient to cause alarm.—J. H. Anderson, *Brit. med. J.*, ii/1926, 682.

Oral use gave correct diagnosis in 92% of 100 consecutive cases. A faint shadow of gall-bladder after giving the dye once does not warrant diagnosis of a pathological gall-bladder. Early cases of cholecystitis may give normal shadows. Occasionally a normal gall-bladder may fail to give a shadow.—P. G. McEvedy and J. E. Sheret, *Lancet*, i/1927, 1120.

Except for 8 complaints of nausea and one case of vomiting, 125 patients were quite unaffected by the drug. The diagnosis was confirmed in 94.3% of cases.—J. H. Mather and W. R. Williams, *Brit. med. J.*, i/1927, 614.

Oral use in the Mayo Clinic good—may well be repeated in doubtful cases. Only a few patients need be submitted to the more uncomfortable and dangerous intravenous method.—G. B. Eusterman, *J. Amer. med. Ass.*, i/1928, 197.

Unpleasant effects from oral use eliminated by mixing the salt with white of egg and then adding to cooked cream of wheat (about 4 ounces). Films as good as by other oral methods.—H. Morris, *Brit. med. J.*, i/1928, 305.

Death coincident with oral use in a man of 62. The relation of the taking of the compound to the onset of acute hepatic degeneration found *p.m.* could not be stated.—G. E. Dyas and S. C. Dyke, *Brit. J. Radiol.*, March, 1928.

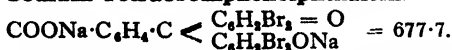
Expulsion of the contents of the gall-bladder in response to fat feeding is a vital function of its musculature and is independent of mechanical factors. General conditions influencing smooth muscle tonus must be considered in interpreting the motor phase of any cholecystographic series.—W. J. M. Scott and L. R. Whitaker, *J. Amer. med. Ass.*, ii/1928, 9.

Administered orally to dogs, even in massive doses, produced no degenerative or necrotic changes in the liver or kidneys.—*J. Amer. med. Ass.*, ii/1927, 196.

There are numerous factors mitigating against efficacy, so that probably not more than 50 to 60% of diagnoses are correct.—T. C. Hunt, *Lancet*, ii/1929, 755.

When it is remembered that the dye is excreted into the bile and the bile containing it is concentrated to a marked degree by the normally-functioning gall-bladder, it will be realised that in this country, where the dye is nearly always given *per os*, the shadow forming shows it is being adequately absorbed from the intestine, that it is being normally secreted by the liver, that the liver secretions are passing freely into the gall-bladder, and that the gall-bladder is adequately concentrating the bile. Too many gall-bladders are being operated upon simply because of absence of a shadow.—A. J. Walton, *Lancet*, i/1930, 338.

### Sodium Tetrabromphenolphthalein.



*Prop. Name.* BROM-TETRAGNOST (Merck, Darmstadt; Martindale, London).

*Dose*.—The dose *per os* is from 4 to 7 g., according to weight of the patient, the average dose being about 5 g.

A pale mauve powder readily soluble in distilled water. Both the powder and solutions should be preserved from the action of the air, as carbon dioxide is slowly absorbed. It has been used for cholecystography, but iodophthalein is now preferred.

### Phenol-Rubrum (B.P.C., U.S.P. XI).

*Syn.* PHENOL RED, PHENOLSULPHONPHTHALEIN.

*Dose*.—(By injection)  $\frac{1}{10}$  grain (0.006 g.). A bright to dark red

crystalline powder slightly soluble in water. Employed as a test for permeability of the kidney. See Vol. II.

## PHOSPHORUS

B.P.C., Fr. Cx., P. Helv. V, P. Dan.

P = 31.02.

[P1] "*Phosphorus, yellow.*"

**Dose.**— $\frac{1}{100}$  to  $\frac{1}{2}$  grain (0.0006 to 0.0025 g.). Fr. Cx. has max. single dose  $\frac{1}{4}$  grain; max. during 24 hours  $\frac{1}{2}$  grain.

Phosphorus is obtained by heating calcium phosphate, sand and coke in the electric furnace, or by converting calcium phosphate (of bones) into the soluble superphosphate by heating with sulphuric acid, this is reduced to metaphosphate by heating with charcoal and finally by further heat is converted into normal calcium phosphate with evolution of phosphorus vapour

A poisonous, non-metallic element melting at 44° and igniting at a slightly greater heat, forming white fumes of phosphorus pentoxide.

**Matches.** The use of yellow phosphorus is prohibited in Great Britain, Germany, etc. "Strike-anywhere" matches usually contain phosphorus sulphide. Safety matches contain an oxidising mixture (potassium chlorate, manganese dioxide, lead peroxide, etc.) on the match and red phosphorus on the box.

Phosphorus necrosis, in consequence of the introduction of the sulphide method of making matches, has entirely disappeared.—Sir Thos. Oliver, *Brit. med. J.*, ii/1925, 530.

**Soluble** about 1 in 320 of absolute alcohol, about 1 in 80 of ether, about 1 in 25 of chloroform, about 1 in 100 each of oleic acid, suet and oils of almond, olive, castor and theobroma, 2 in 1 of carbon disulphide, almost insoluble in water; combines chemically with oils of turpentine and peppermint, forming non-luminous and comparatively non-poisonous liquids.

**Antidotes.** Wash out stomach thoroughly with 1% potassium permanganate solution, using stomach tube. If this is not available give 5 gr. of copper sulphate in water, repeating the dose, first as emetic then as antidote; or use stomach tube with dilute solution of copper sulphate, 15 gr. to 2 gallons of water. Give medicinal charcoal with  $\frac{1}{2}$  oz. of magnesium sulphate, repeating the charcoal frequently. Alkaline drinks and dextrose, but *not* oils, fats or eggs.

**BURNS.**—The best immediate treatment is intermittent immersion of the burnt part in a warm 5% solution of sodium bicarbonate which neutralises the phosphoric acid evolved. The part must be taken out from time to time to allow complete combustion of adherent particles of phosphorus, and treatment must be continued until  $P_2O_5$  can no longer be detected by emission of white vapour or garlicky smell and there is no luminosity in a darkened room.—W. Starz, *Munch. med. Wschr.*, li/1936, 47.

**Uses.** Phosphorus has been given as a nervine stimulant in various affections of the central nervous system and in neuralgia; also in leukaemia, and some skin diseases.

**N.B.** Preparations should be recently made and kept from light.

**[P1] Elixir Phosphori.**

Add compound solution of phosphorus 1 to glycerin 4

*Dose*—15 to 60 minims (1 to 4 ml.) in water. Contains  $\frac{1}{10}$  gr. in 1 dr. A palatable well tolerated "fluid" form of phosphorus

**[P1] Liquor Phosphori Compositus (B.P.C.)** *Syn* TINCTURA PHOSPHORI COMPOSITA.

*Dose*.—3 to 12 minims (0.2 to 0.8 ml.), on sugar

Phosphorus 0.2% *w/v* in chloroform and dehydrated alcohol 12 minims contains about  $\frac{1}{8}$  gr of phosphorus

**[P1] Oleum Phosphoratum (B.P.C.).**

*Dose*.—1 to 5 minims (0.06 to 0.3 ml.), on sugar or in perles

Contains 1% *w/w* of phosphorus in almond oil flavoured with oil of lemon. *P Ital V* is 0.1% in olive oil *P Belg IV* contains no oil of lemon. *P Helv. V* and **[P1] Phosphorus solutus (P.G. VI)** are 0.5% *w/v* in liquid paraffin with ether 2½% *w/v*. *P. Svec X* has 1% in liquid paraffin with 5% of ether.

**ORIENTAL SORE**—Best results in old intractable cases with extensive ulceration, the oil being dabbed on after removing the scab, every other day. When ulcerative process not well developed and lesion is nodular, inject 3 to 5 m hypodermically round or into nodule once or twice weekly, injection practically painless. No general reaction and local reaction slight, but signs of acute inflammation occasionally develop. The delayed action of phosphorus on the liver should be kept in mind—*A. Castellani, J trop Med (Hyg)*, 1925, 377. See also *ibid*, 1923, 194.

**RICKETS and OSTEOMALACIA** and certain cases of very chronic **MALARIAL CACHEXIA**. In these as an adjuvant to quinine and arsenic, a dilute preparation of ½ m of phosphorated oil in 5 m diluent is used—*Brit med J*, 1/1923, 283.

**[P1] Pilulæ Phosphori (B.P.C.)**

*Dose*.—1 to 4 pills. Contain  $\frac{1}{100}$  gr of phosphorus

**[P1] Pilula Phosphori cum Ferro.**

Phosphorated suet 10 gr, reduced iron 150 gr, compound tragacanth powder 10 gr, chloroform 15 m. Mix, and add quickly mucilage of acacia q s. Divide into 50 pills, and varnish. Each pill contains  $\frac{1}{10}$  gr of phosphorus and 3 gr of reduced iron. **[P1 81]** Extract of nux vomica  $\frac{1}{4}$  gr per pill is sometimes added.

**[P1] Pilula Phosphori cum Quinina.**

Made as the preceding with 38 gr of quinine base (= 50 gr of sulphate) in place of the reduced iron.

**[P1 81] Pilula Phosphori cum Strychnina.**

Made as above, with 1½ gr of strychnine, equivalent to  $\frac{1}{10}$  gr per pill.

**Zinci Phosphidum (B.P.C., Fr. Cx.)**  $Zn_3P_2 = 258.2$

*Dose*— $\frac{1}{10}$  to  $\frac{1}{2}$  grain (0.003 to 0.016 g) in pill. *Fr. Cx.* has max single dose  $\frac{1}{2}$  grain, max during 24 hours  $\frac{1}{2}$  grain approx.

A grey powder with slight phosphorus odour. Exerts the same action as phosphorus and can be administered in pills, but is incompatible with acid vegetable extracts (e.g., extract of gentian) owing to liberation of hydrogen phosphide.

**Zoin (Ciba, London)** Water-soluble salt of a complex amino-phosphorus body occurring in milk casein. Contains more than 5% of organic phosphorus. *Dose*—1 or 2 tablets (4 gr) or 1 or 2 ml of liquid Zoin two or three times a day. Neurasthenia, debilitated conditions, etc.

**PHYSOSTIGMA**

*B.P.C.*

*Syn.* PHYSOSTIGMATIS SEMINA, CALABAR BEAN, ORDEAL BEANS.

**[P1]** "Alkaloids, the following, their salts, simple or complex.—Calabar bean, alkaloids of"

[81] "*Alkaloids, the following, their salts, simple or complex — Calabar bean, alkaloids of*"

[86] "*Alkaloids—calabar bean, alkaloids of—specify proportion as the proportion of any one alkaloid of calabar bean that the preparation would be calculated to contain on the assumption that all the alkaloids of calabar bean in the preparation were that alkaloid.*"

*Dose* — 1 to 4 grains

The ripe seeds of *Physostigma venenosum* (Leguminosæ), from West Africa. The poisonous properties are due chiefly to the presence, in the cotyledons only, of physostigmine (up to about 0.25%)

**Antidotes.** Empty stomach by emetic or by stomach tube, using 60 gr of potassium permanganate in 2 gallons of water. Medicinal charcoal or Lugol's solution has been recommended. Atropine sulphate,  $\frac{3}{16}$  gr. hypodermically, is the physiological antidote. Give  $\frac{1}{2}$  oz of brandy or  $\frac{1}{2}$  dr of aromatic spirit of ammonia, in water freely. Strychnine,  $\frac{1}{8}$  gr hypodermically. Artificial respiration may be necessary.

**Uses.** Causes increased peristalsis with liquid motions and excessive urination. Sweating and salivation are produced, the pulse frequency is lessened and blood pressure increased. Preparations of physostigma and solutions of its alkaloid physostigmine  $\frac{1}{4}$  to 1%, applied topically to the eye, contract the pupil, and are antagonistic to atropine. As a miotic the solution acts in 5 to 15 minutes, and the pupils remain contracted for at least 12 hours, usually not returning to normal for two or three days. It is employed to overcome the over-dilatation caused by atropine, homatropine and cocaine. Traumatic tetanus has been well treated with extract  $\frac{1}{8}$  grain every hour then  $\frac{1}{2}$  grain every 2 hours, or physostigmine hypodermically.

[P1 81] **Extractum Physostigmati.**

*Dose* —  $\frac{1}{4}$  to 1 grain (0.016 to 0.06 g.)

An alcoholic extract containing three-fourths of its weight of lactose.

[P1 81] **Tinctura Physostigmati.**

*Dose* — 5 to 15 minims (0.3 to 1 ml.)

Physostigma in no. 40 powder 1, alcohol 90% q.s. to 5.

[P1 81] **Physostigmina.**  $C_{15}H_{21}N_3O_2 = 275.2$  *Syn* ESERINE

*Dose* —  $\frac{1}{1000}$  to  $\frac{1}{300}$  grain (0.0006 to 0.0013 g.)

In colourless crystals, slightly soluble in water, freely in ether, soluble 1 in 180 of soft paraffin, also soluble in other fixed oils. Is used for the preparation of ointments and solutions in oil for use as miotics. For corneal ulcers, [P1 81] solution of 2 gr. per oz. may be dropped into the eye, also in mydriasis and glaucoma.

[P1 81] **Guttæ Physostigminæ Oleosæ (B.P.C.)** Physostigmine (base)  $\frac{1}{2}\%$  in castor oil. Keeps well for ophthalmic use.

Severe frontal headache in young persons due to increased intra-ocular tension, cured by eserine instillations *t.d.s.* — B. L. Raymond, *Brit med. J.*, 1/1934, 103.

[P1 81] **Tablets of Eserine with Trunczek's Serum** (q.v.)

No. 1 contain 0.00025 g eserine in each, with the salts of 50 ml of Trunczek's serum.

No. II contain, in addition to the constituents of No. I, atropine 0.00005 g. in each, for use in the severest forms of intestinal inaction and in obese diabetic patients. Both forms of tablets weigh 8 grains (0.5 g.) each.

Maximum dose of either—6 tablets *per diem*.

[P1-81] **Unguentum Hydrargyri Oxidi Flavi cum Physostigminæ.**

Physostigmine 0.25, soft paraffin 100; heat till dissolved and add, when cold, yellow mercuric oxide 1.

[P1-81] **Unguentum Physostigminæ.** *Syn.* UNGUENTUM ESERINÆ (R.L.O.H.). Physostigmine 1 or 2 gr. dissolved in minimum quantity of chloroform and mixed with yellow soft paraffin (at 61°) to 1 oz.

[P1-81] **Physostigminæ Salicylas** (B.P., U.S.P. XI, P. Austr., Fr. Cx., P.G. VI, P. Helv. V, P. Dan., P. Belg. IV, F.E. VIII, P. Ital. V).  $C_{18}H_{21}O_2N_3, C_7H_5O_2 = 413.2$ . *Syn.* ESERINE SALICYLATE.

*Dose.*— $\frac{1}{100}$  to  $\frac{1}{50}$  grain (0.0006 to 0.0012 g.). Doses of up to  $\frac{1}{50}$  grain (0.003 g.) are sometimes administered. U.S.P. XI average dose  $\frac{1}{30}$  grain.

In needle-shaped or columnar crystals. Soluble about 1 in 100 of water and 1 in 12 of alcohol 90%. Much used as a miotic; solutions are less liable to turn pink than those of the sulphate.

To open the bowels in acute abdominal conditions,  $\frac{1}{100}$  grain hypodermically until 6 doses have been given (4-hourly). This dose is safe—higher dose may act too severely and necessitate bismuth and opium to check the resulting diarrhoea. If no action, give a turpentine enema the following day. The muscular coat of the intestine is directly stimulated by physostigmine.

MYASTHENIA GRAVIS. Physostigmine, being a partial antagonist to curare, was tried in the hope that it would counteract the effect of the unknown substance which might be exerting the curare-like effect on the myoneural junctions. Hypodermic injections of physostigmine salicylate were found to have a striking though temporary effect. Injections of  $\frac{1}{50}$  gr. once daily were of value, but effect wore off in 2 to 4 hours. Greater improvement with  $\frac{1}{50}$  gr., lasting 4 to 5 hours. —M. B. Walker, *Lancet*, i/1934, 1200.

[P1-81] **Guttæ Physostigminæ** (B.P.C.). *Syn.* GUTTÆ ESERINÆ.

Physostigmine salicylate 1% w/v, with boric acid, in distilled water.

[P1-81] **Lamella Physostigminæ** (B.P.). *Syn.* LAMELLA ESERINÆ.

Each contains  $\frac{1}{1000}$  grain (0.000065 g.) of physostigmine salicylate.

[P1-81] **Oculum Physostigminæ** (B.P.). *Syn.* OCULENTUM ESERINÆ.

Contains 0.125% of physostigmine salicylate.

[P1-81] **Physostigminæ Sulphas** (B.P.C., P.G. VI, P. Ned. V, F.E. VIII).  $(C_{18}H_{21}O_2N_3)_2, H_2SO_4 = 648.5$ . *Syn.* ESERINE SULPHATE.

*Dose.*— $\frac{1}{100}$  to  $\frac{1}{50}$  grain (0.006 to 0.0012 g.). (B.P. '14,  $\frac{1}{24}$  to  $\frac{1}{12}$  grain.)

In yellowish, granular, deliquescent crystals, soluble about 4 in 1 of water and 2.5 in 1 of alcohol 90%. Solution becomes pink on exposure, but does not lose much in efficacy.

In doses of  $\frac{1}{100}$  grain (0.0006 g.) of value in tympanites as occurring in typhoid fever.

[P1-81] **Guttæ Physostigminæ (R.L.O.H.)**,  $\frac{1}{2}$ , 1, 2 or 4 gr. to 1 oz. *St. T. H.*, 0 125, 0 25, 0 5 or 1%. *St. M. H.*, 0 25, 0 5 or 1%.

In glaucoma the 0 5 to 1% drops are suited for prolonged use.

The 1% solution instilled 2 or 3 times a day is of value. It contracts the pupils and greatly improves vision—*J. trop. Med. (Hyg.)*, 1926, 303.

[P1-81] **Injectio Physostigminæ Sulphatis Hypodermica**. 1% *Dose*.—1 to 4 minims (0 06 to 0 24 ml.).

[P1-81] **Mistura Physostigminæ Laxativa (B.V.H.)**. Physostigmine sulphate  $\frac{1}{2}$  gr., liquid extract of cascara sagrada 1 dr., ammoniated tincture of podophyllum 15 m., liquid extract of liquorice 15 m., syrup 15 m., compound decoction of aloes to 1 oz.

**Prostigmin (Hoffman-La Roche, London)**. Dimethylcarbamic ester of 3-hydroxyphenyltrimethylammonium-methylsulphate. A synthetic peristaltic stimulant allied to physostigmine, but stable in solution and safer in use. It is given by subcutaneous, intramuscular or intravenous injection in post-operative intestinal paresis, severe constipation, retention of urine, myasthenia gravis, etc. Ampoules of 1 ml. contain 0.5 mg. of active substance.

**MYASTHENIA GRAVIS**. Beneficial results in every one of 7 cases which, though lasting for only a few hours, surpassed anything experienced with other methods of treatment. The injection was given subcutaneously—Prostigmin 2 ml. with atropine  $\frac{1}{100}$  gr. Unpleasant symptoms only of a mild nature.—*L. P. E. Laurent, Brit. med. J.*, 1/1935, 465.

Seven patients treated with Prostigmin, usually 5 ml., in conjunction with atropine sulphate  $\frac{1}{100}$  gr. In each case improvement set in within 5 minutes of the injection, passing off completely in 8 hours.—*E. A. B. Pritchard, Lancet*, 1/1935, 432.

Of the efficacy of eserine, Prostigmin and ephedrine there can be no doubt clinically. It has been suggested that the eserine group, at any rate, may act by stimulating further an already exhausted muscle; there can be no reasonable doubt that this is not the case, and that the eserine group do make the muscles temporarily normal. The observation of Pritchard and Walker that Prostigmin restores the myasthenic myogram to normal is strong evidence that the effect is a genuinely curative one. From the practical point of view it is now possible to abolish the more serious symptoms and to keep the patients in a tolerable state of health by means of ephedrine and eserine or Prostigmin.—*A. M. Cooke and R. Passmore, Quart. J. Med.*, Jan., 1936, 28.

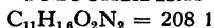
From 25 to 30 mg. of Prostigmin *per os* gives a result comparable in intensity and duration with an injection of 0.5 mg. Two other analogous drugs have also been employed with success: Substance 36 (methyl-phenylcarbamic ester of 3-oxyphenyltrimethyl-ammonium-methyl-sulphate) and Substance 38 (dimethyl-carbamic ester of 8-oxy-methyl-quinolinium-methyl-sulphate). The former has given striking results in a daily dose *per os* of 150 mg. with 30 m of tincture of belladonna given at the same time. It is given in a solution containing 100 mg to the ounce. Improvement is noted from 45 to 50 minutes after taking, reaches maximum intensity in 2 hours and remains maximal for 6 to 8 hours. With 150 mg the intensity of improvement is equal to that observed after injection of 3 mg of Prostigmin. Substance 38, which is given by injection, has an action nearly as intense as that of Prostigmin, but of shorter duration. Experience in 8 cases treated for over a year shows that drugs of this group can be taken without producing unpleasant symptoms or leading to deterioration in the myasthenic condition. The treatment appears to have no direct effect on the ultimate course of the myasthenia, but it improves the general health and patients are able to eat better and to lead a more varied life.—*L. P. E. Laurent and M. B. Walker, Lancet*, 1/1936, 1457.

**PARALYTIC ILEUS** cured by 5 ml of Prostigmin subcutaneously after almost every known remedy (except acetylcholine) had failed.—*W. E. David, Lancet*, 1/1935, 1100.

**Prevention of post-operative ileus with Prostigmin**.—*W. R. Lewis and E. L. Axelman, Amer. J. Surg.*, 1/1936, 308.



## PILOCARPINA



[P1] "*Alkaloids, the following, their salts, simple or complex—Jaborandi, alkaloids of.*"

[81] "*Alkaloids, the following, their salts, simple or complex—Jaborandi, alkaloids of, except substances containing less than 0.5% of the alkaloids of jaborandi.*"

[83] "*Alkaloids—Jaborandi, alkaloids of—in substances containing less than 0.025% of the alkaloids of jaborandi.*"

An alkaloid obtained (0.5%) from *Pilocarpus microphyllus* (Maranham Jaborandi) and other varieties. Easily soluble in water. Soluble in alcohol, ether, chloroform and benzene.

**Antidotes.** Empty stomach by emetic or stomach tube. Give potassium permanganate, 10 gr. in 1 pint of water, by stomach tube, and repeat the dose if necessary. Atropine,  $\frac{1}{15}$  gr., hypodermically, or tincture of belladonna by mouth, this is the specific antidote. Stimulants, e.g., brandy,  $\frac{1}{2}$  oz., or aromatic spirit of ammonia,  $\frac{1}{2}$  dr., in water freely.

**Uses.** A powerful sudorific and sialogogue when administered internally. Large doses have an emetic action. The sweating and salivation commence in about 10 minutes after taking a dose and persist for 2 to 5 hours. Hypodermically it acts in 3 to 5 minutes. It has been given in dropsy of renal origin, but must not be given in cardiac dropsy owing to its depressant action on the heart. It increases the flow of biliary mucus, and has been given to assist the passage of gall-stones. In puerperal eclampsia and uræmic convulsions, it has been given to induce diaphoresis, preferably in conjunction with the external application of heat. In tinnitus aurium (acute labyrinthine) hypodermic injections with gradually increasing dosage are of value in suitable cases. For hiccough small doses every 2 or 3 hours are of value. Salts of pilocarpine have been employed as antidotes to belladonna poisoning, but they do not prevent death from large doses since they only act peripherally.  $\frac{1}{15}$  gr. doses have been given to counteract the effects of hyoscine used in the treatment of morphine addiction by sudden withdrawal. Externally preparations of jaborandi and pilocarpine are used to stimulate growth of hair in alopecia. The 2% solution is used as a miotic; it is less irritating than physostigmine but its action is weaker and more evanescent, miosis lasting for 18 to 24 hours.

**POST-OPERATIVE RETENTION OF URINE.** Pilocarpine *intrav.*  $\frac{1}{2}$  grain, or *per rectum*  $\frac{1}{2}$  grain, often successful where hexamine fails—*per Med Annu.*, 1931, 10. Brief experience favourable.—A. R. Short, *ibid*.

[P1 81] **Pilocarpinæ Hydrobromidum.** *Dose.*— $\frac{1}{2}$  to  $\frac{1}{2}$  grain (0.003 to 0.012 g.) White crystals soluble in water. Used similarly to the nitrate.

### Syrupus Potassii Bromidi et Pilocarpinæ (B.P.C.)

*Dose*—1 to 2 drachms (4 to 8 ml.).

1 drachm contains potassium bromide about  $5\frac{1}{2}$  gr. and pilocarpine hydrobromide  $\frac{1}{15}$  gr. in an orange-flavoured medium.

**Bromocarpine** (prepared in England by *Roberts & Co., London*) is a similar product, stated to have the composition potassium bromide 10, pilocarpine hydrobromide 0.005, orange syrup and glycerin *q s* to 100, by weight. *Dose*—For children 3 to 7 years of age 1 to 3 drachms daily, 7 to 15 years 1 to 6 drachms daily, adults  $\frac{1}{2}$  to 1 ounce daily, *all in divided doses*.

[P1 S1] **Pilocarpinæ Hydrochloridum** (*B P C*, *P G VI*, *Fr. Cx P Ned V*, *P Helv V*, *P Dan*, *P Ital V*, *P Belg. IV*, *FE VIII*)  
 $C_{11}H_{16}O_2N_2 \cdot HCl = 244.6$

*Dose*.— $\frac{1}{10}$  to  $\frac{1}{4}$  grain (0.003 to 0.012 g.) by mouth or hypodermically

In minute, granular, snow-white crystals, slightly deliquescent and very soluble in water. Used similarly to the nitrate

[P1 S1] **Pilocarpinæ Nitras** (*B P*, *U S P XI*, *Fr. Cx*, *FE VIII*, *P Ned V*)  $C_{11}H_{16}O_2N_2 \cdot HNO_3 = 271.2$

*Dose*— $\frac{1}{10}$  to  $\frac{1}{4}$  grain (0.003 to 0.012 g.) *Fr. Cx* has max single dose  $\frac{1}{4}$  grain, max in 24 hours  $\frac{1}{2}$  grain approx. *U S P. XI* average dose  $\frac{1}{10}$  grain

In minute, white, granular, snow-like crystals, but may be obtained in large, white, prismatic crystals. Soluble 1 in 8 of water, but very slightly in cold alcohol

[P1] **Guttæ Pilocarpinæ** (*B P C*) 0.5% of pilocarpine nitrate. Used to contract the pupil of the eye

[P1 S1] **Lamella Pilocarpinæ**.  $\frac{1}{10}$  gr. in a gelatin base

[P1 S1] **Lotio Pilocarpinæ**. For the hair

Pilocarpine nitrate 2 gr., quinine hydrochloride 8 gr., glycerin 2 dr., rose water 6 dr. [P1 S1] Tincture of cantharidin 1 dr. may be usefully combined with above quantities

Applied locally to the scalp, pilocarpine seems to have an action in promoting the growth of hair in alopecia or dandruff. Used also in [P1 S1] **Ointment**, 4 gr. to the ounce of a mixture of wool fat and soft paraffin ointment

[P1 S1] **Sterules Pilocarpine Nitrate** (*Martindale, London*) contain  $\frac{1}{10}$ ,  $\frac{1}{4}$  or  $\frac{1}{2}$  gr.

[P1 S1] **Jaborandi** (*B P C*, *P Helv V*) *Syn* PILOCARPUS.

The dried leaflets of *Pilocarpus microphyllus* (Rutaceæ), containing the alkaloids, pilocarpine (up to about 0.5%), isopilocarpine and pilosine. *P Helv V* describes the dried leaves of *P. Jaborandi*

[P1 S1] **Extractum Jaborandi Liquidum** (*B P C*) 1 in 1

[P1] **Tinctura Jaborandi** (*B P C*)

*Dose*—10 to 30 minims (0.6 to 2 ml.) Liquid extract of jaborandi 1, alcohol 45% to 5

## PILULÆ

**Excipients.** The chief consideration in the preparation of pill masses is the choice of excipient. The following scheme for their preparation is of almost general application.

- When binding material such as gum, fibre, or soft or dry aqueous extracts is present, the ingredients should be massed with syrup or liquid glucose
- When no binding material is present, as in the case of camphor, sulphur, thymol, resins, reduced iron and crystalline substances such as ferrous

sulphate, 5% of compound powder of acacia should be added and the ingredients massed with syrup of liquid glucose. In certain cases it is advisable to substitute liquid glucose for the syrup to give greater cohesiveness.

- (c) Volatile oils and similar substances should be absorbed in powdered curd soap and the mass stiffened with powdered liquorice.
- (d) Oxidising substances such as potassium permanganate should be made into a paste with the minimum amount of wool fat, and the mass stiffened with kaolin or diatomite.

**Coatings.** The practice in vogue in most pharmacies of invariably coating pills, unless otherwise ordered, is advantageous from every point of view. Coated pills are tasteless and elegant in appearance, they are less liable to deteriorate on keeping and are usually more acceptable to the patient than uncoated pills. The following coatings are in general use:—

**VARNISH COATING.** A solution of sandarac in alcohol (95%) 1 in 2 or, for quicker drying, equal volumes of alcohol (95%) and ether. This is the usual form of coating used on the dispensing counter. About 5 to 8 drops of the solution suffice to coat one dozen 5-grain pills.

**SILVER LEAF COATING.** About two leaves are sufficient for twelve 5-grain pills. The pills should be made tacky with dilute mucilage of acacia and then rotated with the silver leaf in a warm, dry, porcelain pot. Silver coating should not be used for pills containing substances liable to affect it, such as sulphides, unless they are previously varnished.

**SUGAR COATING.** This is effected by placing the pills in a hemispherical metallic pan, kept warm while making revolutions, and they are alternately moistened with syrup and dusted with finely-powdered sugar until dry and uniformly covered.

**PEARL COATING.** The pills are first covered with a mucilage of tragacanth (4 grains to 1 fluid ounce with  $\frac{1}{2}$  drachm of syrup), they are then coated by rotating in a pot with French chalk. The operation is repeated several times until a suitable coating has been formed.

**GELATIN COATING.** The pills are held on needles or by suction in a frame, dipped in a solution of 1 part of gelatin in 4 parts of water, and dried. Gelatin coating is very satisfactory.

**Enteric Coatings.** These are coatings designed to render the pills insoluble in the stomach but soluble in the intestines (*see also* glutoid capsules, p. 331). Many substances are used for this purpose, but none of them is perfectly satisfactory. The following are in general use:—

**GLUTOID COATING OR FORMALDEHYDE-GELATIN.** The pills are gelatin-coated in the usual manner, then immersed for 15 minutes in a 2% solution of formaldehyde and dried.

The longer gelatin-coated pills or capsules are immersed in the formaldehyde solution the sooner they disintegrate in an alkaline pancreatic mixture—H. N. Dale, *Pharm. J.*, ii/1932, 494.

**STEARIC ACID.** The pills are rotated in melted stearic acid and caused to roll out on a large sheet of paper so that the coating dries evenly. When the pill mass is of a non-greasy character it is advisable to moisten the pills with a solution of white wax in ether, allowing the latter to evaporate. Unless this is done the coating tends to crack readily and peel off.

**Stearettes** (*Martindale, London*) are tablets made with a coating containing stearic acid with other ingredients to prevent cracking.

**SALOL COATING.** This is applied in the same manner as stearic acid. Non-greasy pill masses should be similarly waxed before coating, otherwise the salol will not adhere.

**KERATIN COATING.** The pills are moistened by rotation in a pot with a 10% solution of keratin in equal parts of alcohol and strong solution of

ammonia, and then shaken out on an oiled tile to dry. The operation is repeated several times and three or four coatings applied.

Coating with Merck's keratin prevented the disintegration of pills in an acid pepsin mixture at 37.5°. Other keratins were unsatisfactory.—H. N. Dale, *Pharm. J.*, ii/1932, 494.

#### Keratinum (B.P.C.).

A group of proteins forming the chief constituents of horns, hoofs, feathers, etc., and resistant to enzyme or chemical action. Occurs as a brownish-yellow powder or greyish-white scales.

[P2] **Liquor Keratini** (B.P.C.) is a 10% w/v solution in ammoniacal alcohol. Used for the enteric coating of pills, capsules, etc.

#### Pulveres pro Pilulis.

It is often possible to prepare from a formula for a pill mass all the ingredients, with the exception of the excipient, in the form of a powder. This facilitates the preparation of repeated batches of the pills, since one weighing of the compound powder will replace three or more in the ordinary manner of dispensing. The following are the relations by weight between the "*Pulvis pro pilulis*" and the quantity of the excipient, syrup of liquid glucose, necessary to produce a pill mass of suitable consistence.

Pill	Weight of powder.	Weight of syrup of liquid glucose.
Pil. Aloes	9	1
" Aloes et Asafœt.	9	1
" Aloes et Ferri .	33	17
" Aloes et Myrrh.	33	17
" Coloc. et Hyoscy.	43	7
" Galbani Co.	3	1
" Hydrarg. Subchlor. Co.	41	5
" Ipecac cum Scilla	5	1
" Plumbi cum Opio	41	6
" Rhei Co.	3	1
" Saponis cum Opio	4	1
" Scillæ Co.	4	1

## PINUS

**Pinus Alba** (B.P.C.). The bark of the Weymouth pine, *P. Strobus* (Pinaceæ).

#### Extractum Pini Albi Liquidum (B.P.C.).

*Dose.*— $\frac{1}{4}$  to 1 drachm (1 to 4 ml.). 1 in 1. Sometimes included in cough syrups.

#### Syrupus Pini Albi Compositus (B.P.C.).

*Dose.*—1 to 2 drachms (4 to 8 ml.).

Liquid extract of white pine, 1 in 20, with syrup of tar, liquid extract of squill and ammonium chloride, in a glycerin-syrup basis.

[P1] **Anodyne Pine Expectorant** (*Parke, Davis, London*). Combination of extracts of white pine, wild cherry, balsam, poplar buds, etc., with chloroform 4 m. and morphine acetate  $\frac{3}{4}$  gr. in 1 oz.

**Pinus Canadensis** (B P C) Syn HEMLOCK SPRUCE, PINUS BARK  
The dried inner bark of *Tsuga canadensis* (Pinaceæ) Contains 8 to 15% of tannin

**Extractum Pini Canadensis Liquidum** (B P C) Dose —  $\frac{1}{4}$  to 1 drachm (1 to 4 ml). 1 in 1 It is used as an astringent in leucorrhœa and given internally for diarrhœa, hæmoptysis and night sweats

**Pinus Sylvestris.** Syn SCOTCH FIR OR PINE

From the wood of this tree (principally in America, France and Russia) much of the oleo-resin, common turpentine, oil of turpentine, gum thus or American frankincense, resin or colophony, and wood tar (*vide* Pix Liquida) are produced From its leaves also are prepared an extract and volatile oil

**Oleum Pini Sylvestris** is a commercial name for the oil distilled from various coniferous leaves and twigs, it is not distilled from *Pinus sylvestris*

**Oleum Terebinthinæ** (B P, U S P XI, P Helv V, P Dan, Fr Cx) Syn OLEUM TEREBINTHINÆ ÆTHERFUM (Fr Cx), OLEUM TEREBINTHINÆ RECTIFICATUM, CAMPHINE

Dose — 3 to 10 minims (0.2 to 0.6 ml) Anthelmintic dose 2 to 4 drachms (8 to 16 ml)

Is distilled from the oleo-resin, turpentine, obtained from *Pinus sylvestris* and other species of *Pinus* U S P XI and P Helv V contain Oleum Terebinthinæ and Oleum Terebinthinæ Rectificatum, the latter to be dispensed when for internal use Fr Cx, P Helv. V and P Dan recognise the oil of *P. maritima* (P Pinaster) only

**Soluble** 1 in 7 of alcohol 90%, miscible with alcohol 95%, ether, chloroform and glacial acetic acid

By "Turpentine," *i.e.*, **Terebinthina** (N F VI, P Stec X and in other countries), is meant the concrete oleo-resin obtained as exudate from various species of *Pinus* Synonyms for this natural product are gum thus, Thus Americanum and common frankincense **Bordeaux Turpentine** is a variety obtained in S W France

**Antidotes.** Empty stomach by emetic or stomach tube Give purgative dose of magnesium sulphate. Demulcent drinks Hot applications to loins Morphine,  $\frac{1}{4}$  gr hypodermically, or tincture of opium by mouth, for pain.

Death of a man of 39 following drinking of 6 oz. of oil of turpentine Lining of stomach completely macerated and lying in small pieces in the gastric cavity The wall of the stomach felt like leather — F P Mantland, *Brit med J*, 11/1931, 77

**TURPENTINE IDIOSYNCRASY** Vesicular eruption, urticaria and vomiting following use of Linimentum Album (B P C) on unbroken skin — W W Jeudwine, *Brit med J*, 1/1933, 513

Idiosyncrasy by no means unusual Turpentine causes rubefaction and vesiculation on any skin if applied sufficiently concentrated, and will cause this irritation in some individuals in very small dosage, the irritation in these cases not being limited to the site of application, but a papular, urticarial rash, which may become oozing and eczematous, appears at the periphery of the point of contact and may become quite generalised The application of turpentine to the skin contains a real element of danger — R L Sutton, *Brit med J*, 1/1933, 805; J T Ingram, *ibid*, 894

**Uses.** Oil of turpentine has the therapeutic action of other essential oils. Internally it is carminative, producing a sensation of warmth in the mouth and stomach and assisting the expulsion of flatus It is excreted especially by the kidneys and lungs, and is given in cystitis as an antiseptic and for promoting diuresis, and in bronchitis as an expectorant Large doses are irritant to the

bladder and urethra and even small doses may increase a pre-existing inflammation. Given with castor oil to prevent absorption, large doses are administered as a vermifuge for tape-worm. As an enema it is employed to evacuate the bowel, to expel flatus and also to remove tape-worm and thread-worm. Mixed with olive oil it is of value as an enema in the tymanites of typhoid fever. Externally it is rubefacient, and is employed in numerous liniments for rheumatism, stiffness, etc., and a turpentine stupe consisting of  $\frac{1}{2}$  to 1 dr. of the oil sprinkled on flannel wrung out of hot water is commonly used as a counter-irritant for the relief of abdominal pain. The oil is an effective hæmostatic, and may be applied on gauze to arrest hæmorrhage from a tooth socket or the nose. It has been given in 10 m doses orally for internal hæmorrhage, but its value is uncertain (*see* 19th Edn, p. 699).

Subcutaneous or intramuscular injections of turpentine are given to promote the formation of a "fixation abscess" in the treatment of various diseases of microbial origin. The oil may be given as a 15% admixture with olive oil, sometimes with the addition of 0.5% each of benzocaine and quinine hydrochloride. The adult dose is 0.5 to 1 ml every 4 to 7 days, children may receive 4 m, and infants up to 5 years 1 to 2 m weekly. Increased leucocytosis is produced, and the treatment has been found valuable in septicæmia, erysipelas and other streptococcal infections, also in furunculosis, acne, etc. Fixation abscess treatment may also assist in the isolation of the infecting organisms in infections of unknown origin.

Turpentine injections (10% to 20% in olive oil) at Mount Sinai Hospital. The site selected was the intersection of a horizontal line drawn from the posterior axillary border and a line one or two fingers' breadth below the brim of the pelvis. At this part the needle easily strikes the periosteum, upon which the injection is made. Good in some cases of acne, especially good in ulcer of the leg—*Med. Rec.*, Jan. 14, 1922, *Practitioner*, 11/1922, 188, *trop. Med. (Hyg.)*, 1923, 197.

Chilblains of the legs treated with turpentine injections.—*Brit. med. J.* 1/1925, 1194.

**TYPHOID.** Give 20 m of turpentine emulsion or a capsule of 5 m oil of cinnamon 2- or 4-hourly and a  $\frac{1}{2}$  pint ox-gall enema, and apply heat to the abdomen if there is no hæmorrhage.—A. E. Gow, *Lancet*, 1/1930, 39.

**Emulum Olei Terebinthinæ (U.S.P. XI).** Average dose— $\frac{1}{2}$  drachm (2 ml). Rectified oil of turpentine 15% with acacia and water.

**Enema Terebinthinæ (B.P.C.).** Dose—20 ounces (600 ml). Oil of turpentine 2.5 to 5%, v/v in mucilage of starch or in 5% aqueous soft soap.

**Enema Terebinthinæ (St. M.H., St. Mark's H.).** Oil of turpentine  $\frac{1}{4}$  oz., soap enema (1 in 20) to 1 pint. *W.H.* is the same except that the soap enema is 1 in 40. *St. T.H.* uses oil of turpentine  $\frac{1}{4}$  to  $\frac{1}{2}$  oz. in  $\frac{1}{2}$  to 1 pint of mucilage of starch. *St. G.H.* has oil of turpentine 1 oz. in starch enema ( $\frac{1}{4}$  oz. boiled with 20 oz. of water) to 1 pint. *Mid. H.* has 1 oz. of oil in 20 oz. of simple enema (soft soap 1 oz., water to 1 pint). *L.H.* is the same, using  $\frac{1}{4}$  to 4 dr. of oil. *K.C.H.* uses 1 oz. of oil of turpentine emulsified in milk 2 oz., or yolk of egg, and made up to  $\frac{1}{2}$  to 1 pint with soap enema (1 in 20). *St. Orm H.* uses 2 dr. of oil mixed with 10 oz. of starch mucilage prepared with 2 dr. of starch. *C.X.H.* has oil of turpentine 1 oz., starch enema (1 in 40) to 15 oz.

**Gossypium Terebinthinæ.** *Syn.* TURPENTINE WOOL (*R.D.H.*) Cotton wool or gauze soaked in the oil and squeezed dry, packed into the tooth socket as a stupe.

**Hustus Terebinthinæ** (*St GH*). Oil of turpentine 10 m, tincture of quillaja 10 m, syrup 30 m, cinnamon water to 1 oz

**Linimentum Album** (*B.P.C*). *Syn.* EGG LINIMENT, WHITE EMBROCATION, LINIMENTUM ALBUM ACETICUM.

An egg emulsion containing about 40% of oil of turpentine and 8% of acetic acid.

**Lin. Album** (*N.I.F.*). *Syn.* LIN COMMUNE. Soft soap 66 gr, ammonium chloride 11 gr, oil of turpentine  $\frac{1}{2}$  oz., hot water to 2 oz.

**Linimentum Terebinthinæ** (*B.P.*).

Contains oil of turpentine 65% *v/v* with camphor 5% *w/v*, soft soap and distilled water.

Knight's method is satisfactory Mix solution of potash (*B P* '98) 3 oz. with water 3 oz. in a bottle, add oleic acid 7 dr. previously mixed with oil of turpentine 3 oz, and mix gently To this emulsion add oil of turpentine 10 oz with camphor 1 oz dissolved in it, in portions of 1 oz or more at a time. Liquor Potassæ (*B P* '98) contained 6.19% *w/v* of KOH.

**Linimentum Terebinthinæ Aceticum** (*B.P.*)

Glacial acetic acid 110 ml, liniment of camphor 445 ml., oil of turpentine to 1000 ml.

**Linimentum Terebinthinæ Aceticum** (*N F. VI*) *Syn* STOKES' LINIMENT ST. JOHN LONG'S LINIMENT Oil of turpentine 400 ml, oil of lemon 16 ml, acetic acid 80 ml, yolks of 4 eggs, whites of 2 eggs, water to 1000 ml

**Linimentum Terebinthinæ Compositum** (*B V H*) Salicylic ester of dihydroxy-ethane 1 oz, oleoresin of capsicum 5 gr, olive oil 2 oz, oil of turpentine to 5 oz

**Dutch Drops.** *Syn.* HAARLEM DROPS. For lumbago and rheumatism.

*Ph* Form states —Form now generally adopted in Denmark and Holland is —Heat to 165° in an iron vessel large enough to allow some frothing, linseed oil 4 and sulphur 1, with stirring until mixture drops off the stirrer with a glassy appearance Remove from the fire and add 15 parts (by weight) of oil of turpentine, and agitate until solution is complete or nearly so, then filter The liquid should be limpid and of a brownish-red colour

**Sapo Olei Terebinthinæ.**

Turpentine 1, soft soap 2, glycerin 1 As a vermicide—also a stimulant local application.

**Spiritus "Antiparalyticus."** Turpentine oil 4, oil of amber 4, camphorated spirit 64, dilute solution of ammonia 28 Used as a liniment

**"Sanitas" Fluid** (*Sanitas Co., London*) is prepared by the action of water upon air-oxidised turpentine It contains as its active principles hydrogen peroxide, thymol, a soluble camphor, and some camphoric acid A household disinfectant and oxidiser. Non-poisonous, does not stain linen Is used in midwifery. **"Sanitas" Oil** has sp gr 0.95 A strong oxidising agent For inhalation in phthisis. Diluted with spirit used as spray in a room, or 1 in 8 to 20 of olive oil for skin affections

**Sterules of Rectified Turpentine in Olive Oil** (*Martindale, London*) contain 1 and 2 ml of 15% solution

**Terpichin** (*Ostreicher, Berlin; C Zimmermann, London*) Ampoules containing oil of turpentine and quinine in oily solution

**Terebinthina Canadensis** (*B.P.C*). *Syn.* CANADA BALSAM, BALSAM OF FIR.

The oleoresin from *Abies balsamea* (*Pinacæ*) occurring as a pale yellow, viscid liquid soluble in all proportions of benzene,

xylene, chloroform and ether; about 80% is soluble in alcohol 90%. After preparation by warming for some hours in an open dish until a small portion sets to a brittle solid on being cooled, and dissolving the residue in an equal quantity of xylene it is used as a microscopic mounting medium.

**Venice Turpentine** is the oleoresin from *Larix europæa* (Pinaceæ) It is a viscid yellow fluid soluble in dehydrated alcohol

**Terebinthina Veneta** (P. Helv. V) is from *L. decidua*

Commercial Venice turpentine is usually a factitious substance.

**Alcoolat de Fioraventi.** Syn BALSAMUM FIORAVENTI (Fr. Cx)

Venice turpentine (Térébenthine de Mèlèze) 10, elemi 2, storax 2, galbanum 2, myrrh 2, laurel berries (baies de laurier) 2, aloes 1, galangal 1, ginger 1, zedoary 1, cinnamon (cannelle de Ceylan) 1, clove (girofles) 1, raisins (muscades) 1, *Origanum Dictamnus* flowers (dictame de Crète) 1, alcohol (80%) 60. Macerate 2 days *s a* and distil to obtain 50. It is used as an embrocation in rheumatism.

For alopecia, Liquor Ammoniae 1, baume fioraventi 15, spirit of camphor 15. Apply with friction after washing with soap.

**Balsamum Locatelli.** Venice turpentine 18, yellow beeswax 12, olive oil 18, balsam of Peru 2, dragon's blood 1. For chilblains (even if broken)

**Terebinthina Veneta Factitia** (B.P.C.) A mixture of colophony, linseed oil and oil of turpentine melted together and allowed to cool

**Larix** (B.P.C.) Syn LARCH BARK

The bark of *Larix europæa*, containing tannin. **Tinctura Laricis**, dose — 20 to 30 minims, 1 in 8, has been used as an expectorant in chronic bronchitis

**Oleum Pini Pumilionis** (B.P.C., U.S.P. XI, P. Helv. V).

Dose — 1 to 5 minims (0.06 to 0.3 ml.).

The oil of the leaf of *Pinus Pumilio* (Coniferae) Is more aromatic than the oil of Siberian fir. It is used for inhalations

**Syrupus Pini** (B.P.C.)

Dose —  $\frac{1}{2}$  to 1 drachm (2 to 4 ml.).

Contains 1 in 160 of oil of pumilio pine in glycerin, sucrose and water

[D.P. 81] **Linctus Pini, Terpin et Heroin** (Martindale, London) A preparation of oil of pumilio pine with  $\frac{1}{16}$  gr of diamorphine hydrochloride and  $\frac{1}{4}$  gr of terpine hydrate per dr in a glycerin, alcohol and syrup menstruum. Dose — 1 drachm.

[D.P. 81] **Pinheroin** (Oppenheimer, London) Preparation containing diamorphine hydrochloride  $\frac{1}{16}$  gr and terpine hydrate 1 gr per dr with essence of Canadian pine, for use as a respiratory stimulant. Dose — 1 drachm every 2 or 3 hours if necessary

**Oleum Abietis** (B.P.). Syn OIL OF SIBERIAN FIR, OIL OF PINE. Distilled from the fresh leaves of *Abies sibirica*. Contains 35 to 45% w/w of esters calculated as bornyl acetate,  $C_{12}H_{20}O_2$

MOSQUITO LARVÆ AND PUPÆ. Pine oil has a powerful soporific or paralysing effect, resulting in their death. A mixture of crude oil and pine oil, in the proportion of 9 parts of the former to 1 of the latter, is effective in destroying all stages of Anopheline and Culicine larvæ and pupæ.—Per J. Amer. med. Ass., 11/1925, 221.

**Olibanum** (B.P.C., P. Dan.), syn. FRANKINCENSE, is the dried oleoresin from *Boswellia Carteri* and other species (Burseraceæ). In ovoid yellowish, bluish or greenish tears. Used in incense and fumigating powders.

**Terebenum** (B.P., U.S.P. XI)

Dose.—5 to 15 minims (0.3 to 1 ml.). U.S.P. XI average dose 4 minims.



A colourless liquid consisting of dipentene and other hydrocarbons, produced by the action of sulphuric acid on oil of turpentine and distillation. Sp. gr. 0.862 to 0.870. It has an agreeable odour resembling fresh-sawn pine-wood

**Soluble** 1 in 5 of alcohol 90% and in all proportions in absolute alcohol or chloroform. It is not miscible with water, but may be emulsified by mixing it with one-sixth its weight of tragacanth powder, then adding water and shaking.

**Uses.** An agreeable antiseptic, disinfectant and deodoriser. The vapour is a useful sedative and antiseptic inhalation in whooping cough and in hay fever. 5-minim capsules or pastilles are made. Useful *per os* in dysentery. In excess it may produce albuminuria and hæmaturia.

WHOOPING COUGH cured by 1 to 2 minims on sugar occasionally—*Lancet* 11/1929, 34

**Vapor Terebeni.** Equal parts of terebene, phenol and spirit of chloroform 10 drops on the pad of an oro-nasal respirator

**Bronchol** (*Sharpe & Dohme, London*) Capsules containing terebene 1 m., oil of sandalwood  $1\frac{1}{2}$  m., creosote  $\frac{1}{2}$  m., eucalyptol 1 m., strychnine  $\frac{1}{10}$  gr., olive oil to 5 m. For bronchitis, bronchial catarrh, etc. *Dose*—1 or 2 capsules after meals

**Terpini Hydras** (*B P C, U S P XI, Fr. Cx, P. Hung, P. Ned V, P. Helv. V, P. Belg. IV*)  $C_6H_8(OH)_2 \cdot CH_3 \cdot C_3H_7, H_2O = 190.2$  *Syn.* TERPENE, TERPENE HYDRATE.

*Dose.*—3 to 10 grains (0.12 to 0.6 g.), in cachets, capsules or pills, or suspended in a mixture.

In prismatic crystals

**Soluble** 1 in 280 of water, 1 in 32 of boiling water, 1 in 14 of alcohol 90%, 1 in 100 of ether, 1 in 200 of chloroform

**Uses.** Lessens cough, has been used with success in bronchitis, chronic and subacute, it assists expectoration, *e.g.*, in initial catarrh of phthisis, useful as a hæmostatic in bleeding from lungs. Diuretic

**Terpinol**,  $C_{10}H_{18}$ . *Dose*— $1\frac{1}{2}$  minims (0.1 ml.) or more in pill, or gelatin capsule. An agreeably aromatic liquid containing various terpenes, obtained by the action of dilute sulphuric acid on terpin hydrate. Miscible with alcohol in all proportions, but insoluble in water. Has been given in pulmonary hæmorrhage in 3-drop doses. Is used mainly in perfumery for its hyacinth odour

**Terpineol**,  $C_{10}H_{17}OH = 154.1$  *Syn.* TERPINENOL. A colourless viscid liquid obtained by the fractional distillation of terpinol. Used for disguising odour of iodoform and in perfumery, having a lilac odour

**Terpoflor** (*Wilcox, Jozeau, London*). Contains cedrene, pinene, anethol, camphoric aldehyde, cineole, methyl orthoamidobenzoate, linalyl acetate, terpineol and sesquiterpenes in liquid paraffin. Supplied in gelatine capsules, the contents of which are instilled into the nose. For use in nasal congestion

## PITUITARIUM

*Syn.* PITUITARY GLAND, HYPOPHYSIS CEREBRI

[P1] "Pituitary gland, the active principles of"

[86] "Pituitary gland, the active principles of—specify proportion as either -

- (a) *the number of units of activity as defined in the "British Pharmacopœia" contained in a specified quantity of the preparation, or*
- (b) *the proportion of pituitary gland, or of anterior or of posterior lobe of the gland, as the case may be, contained in the preparation; or*
- (c) *the amount of pituitary gland, or of anterior or of posterior lobe of the gland, as the case may be, from which a specified quantity of the preparation was obtained, together with an indication whether the amount relates to fresh or to dried gland substance "*

[87] *Medicines made up ready for the internal treatment of human ailments containing—Pituitary gland, the active principles of—must be labelled with the words "Caution It is dangerous to take this preparation except under medical supervision "*

A small reddish-grey, ductless gland weighing, in man, about 10 grains, situated at the base of the brain in the sella turcica of the sphenoid bone. The average total weight of the gland in the ox is 2.5 g; the anterior part being 2 g, and posterior 0.5 g

**Anatomically** the gland consists of the anterior lobe, the *pars intermedia*, the posterior lobe and the *pars tuberalis*. The *pars intermedia* lies between the (larger) anterior lobe and the (smaller) posterior lobe, it is developed in connection with the anterior lobe as an upward growth (Rathke's pouch) of the ectoderm lining the bucco-pharyngeal cavity. The posterior lobe is developed from that portion of the diencephalon which forms the floor of the third ventricle with which it is connected by the neck or infundibulum (a funnel). In man, both neck and body are solid, with traces of a cavity in the neck. The *pars tuberalis* is a thin layer which forms a collar for the infundibulum, and spreads out over a small adjacent part of the base of the brain.

**Histologically** the anterior lobe is composed of irregular columns of cells separated by connective tissue and large vascular sinuses. The cells are large, polyhedral with round central nuclei, and are differentiated into two groups according to the intensities of the staining reactions of their cytoplasm—chromophobe cells with clear non-granular cytoplasm and chromophil cells with deeply staining granules—further differentiated as acidophil (oxyphil) and basophil cells, according to the affinities of their cytoplasm for acid and basic dyes respectively. The posterior lobe, or *pars nervosa*, is composed of neuroglia cells, fibres and pituicytes, but no nerve cells have been identified in it. In the human pituitary gland the bulk of the tissue of the posterior lobe is made up of larger pyramidal or spindle-shaped cells termed pituicytes, which often contain greenish-brown granules. The *pars intermedia* is closely applied to the *pars nervosa*, and consists of short columns of small polyhedral cells with round, centrally-placed nuclei and granular cytoplasm.

**Physiologically** the resemblance of the minute structure of

the anterior portion of the gland to a typical secreting gland is consistent with the production of an internal secretion, but the resemblance of the cells of the *pars nervosa* to those of nervous tissue has led to the suggestion by many investigators that the secretion of the posterior lobe is elaborated in the *pars intermedia*.

**Functions of the Pituitary Gland.** The name pituitary (pituita = mucus or phlegm) perpetuates the old belief that the function of this gland was to secrete the nasal mucus. The manifold functions now assigned to it have led to its description as the "master-gland," or "leader of the endocrine orchestra" (Langdon Brown). It has a direct influence on the action of the thyroid, pancreas, adrenals and sex-glands.

Animal experiments indicate that the pituitary produces in addition to the gonadotropic and thyrotropic fractions both an insulin-stimulating and an insulin-antagonising hormone, a parathyrotropic hormone and an adrenotropic hormone. The position seems to be that the anterior pituitary gland exerts a controlling influence on the whole endocrine system — *Brit med. J.*, 1/1934, 628

Injection of 2 ml per kg. of pituitary (posterior lobe) extract in the rabbit causes temporary inhibition of the secretion of hydrochloric acid, preventing the usual response to histamine for 6 hours. A severe anæmia may develop after some days. There appears to be a connection between the posterior lobe of the pituitary, the stomach and the blood picture — E. C. Dodds and others, *Lancet*, 1/1935, 1099.

The hypophysis and metabolism (with a bibliography containing 437 references). — B. A. Houssay, *New Engl J Med*, 1/1936, 961

### Posterior Lobe

[P1-87] **Extractum Pituitarii Liquidum (B P)** *Prop Names.* GLANDUITRIN (*Richter, London*), HYPOPHYSIN (*Bayer Products, London*), INFUNDIBULIN (*Evans, Sons, Lescher & Webb, Liverpool*), INFUNDIN (*Burroughs Wellcome, London*), PITIBULIN (*Allen & Hanburys, London*), PITOXYLIN (*Oxo, London*), PITUITRIN (*Parke, Davis, London*).

*Dose.*—2 to 5 units (0.2 to 0.5 ml) by subcutaneous injection

Pituitary (posterior lobe) extract is prepared with 0.25% acetic acid, and is assayed and adjusted to contain 10 units per ml and to pH 3.

[P1-87] **Liquor Pituitarii Posterii (U.S.P. XI).**

*Average dose.*—15 minims (1 ml), by hypodermic injection

1 ml produces an activity upon the isolated uterus of the virgin guinea-pig equal to 80 to 120% of that produced by 0.005 g. of a standard powdered posterior pituitary.

**International Standard Preparation.** Adopted by the League of Nations Commission on the Standardisation of Sera, Serological Reactions and Biological Products; it is a dry preparation of the acetone-extracted fresh posterior lobe substance of ox-pituitary, and is used for the biological evaluation of preparations

of the posterior lobe of the pituitary, whether containing all the active principles of the lobe or the pressor or oxytocic principle in separate solution

**Therapeutic Substances Regulations.** The standard preparation is kept at the National Institute for Medical Research, Hampstead. The *unit* is the activity corresponding to that yielded by 0.5 mg of the *standard preparation* when extracted by an approved method. The acidity of the aqueous extract shall be not less than pH 5 nor more than pH 4. Samples must be tested for sterility, and the label must indicate the strength (units per ml), batch number and licence number, and name and address of manufacturer

The *BP* directs that extracts should not be used when more than 18 months old.

The statement in the *BP* as to the reduction in activity during storage is only correct if the average temperature does not rise above 5°.—F Wokes, *Pharm J*, 11/1932, 476

**Hypersensitiveness to pituitary extracts** occurs in only a small percentage of persons. The constituent of the extract responsible is neither the vasopressor nor the oxytocic principle. The symptoms are usually swelling of the face and hands with urticaria.—Senior and Ryder, *J Amer. med Ass*, 1/1936, 512

Spasm of the cervix which on rare occasions occurs with retention of the placenta after the proper use of pituitary extract may be relieved by injection, of 5 m of adrenaline solution 1 : 1000.—G G Copeland, *Canad med Ass. J.*, 1/1936, 317

**Uses.** Pituitary (posterior lobe) extract is used to stimulate uterine contractions in labour. Used judiciously it is of distinct value, but used indiscriminately, when the *os uteri* is not fully dilated, it may be dangerous and cause rupture of the uterus. Good results are claimed by giving a tablespoonful of castor oil in the morning, and injecting 2 drops pituitary extract solution hourly throughout the day. By this procedure labour is stated usually to terminate in 18 hours.

Pituitary (posterior lobe) extract is also used to control post-partum hæmorrhage and to stimulate contraction of intestinal muscle in post-operative intestinal stasis, though according to some authorities it has very little direct stimulant action on the intestinal muscle and its effect may be secondary to an increased outflow of bile. Further uses are to raise blood pressure in surgical shock, also to counteract the fall in blood pressure sometimes occurring under spinal anæsthesia, to control polyuria in diabetes insipidus, and to overcome the effects of an overdose of insulin

Effect of pituitary (posterior lobe) extract on blood pressure. Doses of 10 units of pituitary (posterior lobe) extract given intramuscularly to 62 persons gave no constant changes in blood pressure. In the majority there was no change, in a few the pressure was raised, in others it was lowered. Comment—*Lancet*, 1/1934, 1124.

**CARDIAC STIMULANT.** As a temporary cardiac stimulant in acute diseases, such as pneumonia, pituitary (posterior lobe) extract has been found successful when strychnine and camphor have failed.—G. R. Murray, *Clin J*, Aug, 1923, 364

**CONSTIPATION** due to morphine corrected by 1 ml. of extract.—E Obermer, *Brit med J*, 1/1926, 17.

The use of pituitary extract to promote peristalsis in young infants is fraught with danger, since it readily produces intussusception.—J. A Foote, *J Amer med Ass*, 11/1925, 722

**DIABETES INSIPIDUS.** Pituitary (posterior lobe) causes a marked antidiuretic effect lasting some hours in patients with diabetes insipidus or in normal subjects who have previously drunk large quantities of water. This effect is believed to be a direct action on the kidney, and to be due to an increased reabsorption of water by certain cells of the tubule.—See W W Burgess, A M Harvey and E K Marshall, *J Pharmacol*, 1933, 19, 237. See also I Gersh, *J Pharmacol*, 1934, 52, 231.

Posterior lobe extract 1 ml subcutaneously of value in diabetes insipidus—P. Carnot and M Peron, *Paris méd*, Oct., 1925, 339.

Intranasal administration of 1 ml liquid extract applied with a spray (also by insufflation of powder) successful in many cases of diabetes insipidus—Per *Brit med. J Epit*, 11/1928, 82, also *ibid*, 1/1929, 21.

**DIABETES MELLITUS.** Subcutaneous injections of pituitary (posterior lobe) markedly antagonise the effect of insulin on blood-sugar in normal and diabetic individuals—R D Lawrence and R F L Hewlett, *Brit. med. J*, 1/1925, 998.

In the early days of research into the action of insulin it was considered that this hormone was responsible for keeping gluconeogenesis within bounds, but it has now been shown that if the pituitary gland is removed from a dog after the pancreas has been removed the principal signs of diabetes disappear (*i.e.*, excessive gluconeogenesis is not in evidence). Our conception of diabetes must be modified to include most of the endocrine glands and the pituitary must now be considered as a fundamental factor—*Brit med J*, 1/1934, 112.

It would appear doubtful whether either of the posterior pituitary hormones is of any significance in determining the blood-sugar level in rabbits. While hyperglycæmia does follow the administration of the pressor substance, the dosage necessary is too high to be considered physiological—H C Ellsworth, *J Pharmacol*, 1935, 11, 435.

**ENURESIS** in children well treated with injections of pituitary extract—Per *J Amer med Ass*, 11/1925, 1434.

**HÆMOPTYSIS.** The most effective immediate remedy is the subcutaneous injection of 1 ml of pituitary (posterior lobe) extract—W H Wynn, *Brit med. J*, 11/1934, 833.

**HERPES ZOSTER.** Relief of pain following injection of 1 ml. It appears to act most dramatically when the pain is most intense—F H Gillett, *Lancet*, 11/1934, 307.

**LABOUR.** Its use during labour—W Blair Bell, *Brit med J*, 1/1925, 1027. Action on the uterus—*Lancet*, 11/1926, 343.

When pituitary is used to induce labour it should not be repeated once pains are established, otherwise great danger is incurred—W A Scott, per *Prescriber*, 1928, 180.

Ampoules containing only 2 units should be available, as this dose appears safe at any stage, providing there is no mechanical obstruction, and if given before the os is half dilated, hastens course of sluggish labour—A W Bourne and J H Burn, per *Brit med J*, 1/1928, 273, *Pharm J*, 1/1928, 125.

Its effect may last longer than an hour, which is the least interval at which a dose can be usefully repeated—A Bourne and J H Burn, *Pharm J*, 11/1927, 485. See also *Lancet*, 11/1927, 560, *J Obstet Gynec*, 11, 249, and *Pharm J*, 1/1927, 133.

Pituitary extract not suitable in cases of primary inertia—O'D Browne. No place for it in second stage and likely to produce hour-glass contraction in third stage, but of great value after labour is complete—F J Cunningham. Should not be given until after uterus is empty.—R M. Corbet. Administration of pituitary extract has no place in labour—A H Davidson. Nearly the only time for pituitary was after completion of the third stage. Many cases of rupture of the uterus due to its use in labour.—B Solomons, *Disc Sect of Obstet*, *Roy Acad of Med. in Ireland*, *Brit. med J*, 1/1933, 370.

The multipara with the flabby uterus must not be given any oxytocic drug. It is safer for the general practitioner to reserve pituitary extract for the termination of the third stage.—B. Solomons, *Lancet*, 11/1934, 11.

The action of the uterine muscle to pituitary preparations is markedly affected by the nature of that ovarian, placental or anterior pituitary hormone whose influence is predominant at the time of injection. During the early stages of pregnancy the human uterus does not react to Pitocin, probably because of the inhibitory effect of the luteal secretion. It does, however, respond to small doses of Pitressin; whether this is an effect of the drug *per se* or is due to

mechanical factors remains a moot point. Later in the gestation period the reactivity to Pitocin returns, and during parturition the uterus is very reactive to this substance, and also to solution of pituitary,—E. M. K. Geeling, *J. Amer. med. Ass.*, 1/1935, 738

Nasal method of administration safe and efficient for accelerating labour already in progress. Insert a pledget of cotton wool moistened with 20 m. pituitary extract under the anterior end of the inferior turbinate of one nostril, withdraw after an hour or two and, if necessary, apply a fresh pledget to the opposite nostril.—Hofbauer and Hobiner, per *Prescriber*, 1928, 180

Intravenous injection of pituitary (posterior lobe) extract in doses of 1 minum given in a number of cases, said to be safe. Best results when given after the membranes have ruptured and in secondary inertia, before full dilatation or with full dilatation when the head is on the perineum, results also good in post-partum hæmorrhage and after cesarean section.—H. A. Barron, *J. Obstet. Gynec.*, 1935, 322. See also *Lancet*, 1/1935, 1398

The dangers of use in obstetrics.—M. Pierce Rucker, *J. Amer. med. Ass.*, 11/1925, 1637

Intravenous injection in the third stage of labour. The interval between the birth of the fœtus and the passage of the placenta was reduced by one-half, and the loss of blood was also diminished by almost one-half in injected patients.—Per *Prescriber*, 1927, 193

After intravenous injection of pituitary (posterior lobe) extract, the non-pregnant uterus shows no change in consistency, but the pregnant uterus shows a marked increase in consistency—said to be helpful test for pregnancy, though not conclusive.—M. R. White and J. P. Pratt, *Endocrinology*, 1936, 17

MIGRAINE well treated by 0.5 ml. intramuscularly once weekly—prolonged improvement.—*Brit. med. J. Epit.*, 1/1928, 92

PARALYTIC ILEUS. Pituitary (posterior lobe) intravenously extremely valuable, given in a dose of 0.5 to 1 ml. into the median antecubital vein very slowly (0.1 ml. every 5 seconds). Dramatically sudden result in every one of three cases.—F. F. Rundle, *Brit. med. J.*, 11/1935, 1208

POST-PARTUM HÆMORRHAGE. In cases of post-partum hæmorrhage, pituitary (posterior lobe) extract should be injected into the fundus uteri through the abdominal wall, provided the bladder is empty. The uterus must be compressed bimanually, a fist being inserted into the anterior fornix and the external hand behind the organ pressing it forwards and upwards. W. F. Rawson, *Brit. med. J.*, 1/1935, 1317

SERUM SHOCK AND SERUM SICKNESS well treated with pituitary extract or adrenaline solution 1 ml.—W. M. Crofton, *Prescriber*, 1923, 235

### SOME PROPRIETARIES CONTAINING PITUITARY (POSTERIOR LOBE) EXTRACT

[P1 87] **Chinuitrin** (*Richter, London*). Quinine bihydrochloride 0.3 g., urea 0.1 g. and posterior lobe extract 10 units. Dose—1 ml. daily subcutaneously or intramuscularly. Uterine inertia, post-partum hæmorrhage

[P1 87] **Lysasthmin** (*Richter, London*). Glanduitrin (posterior pituitary extract) 0.5 ml., adrenaline (1 in 1000) 0.5 ml. Dose—0.5 to 2 ml. subcutaneously or intramuscularly. Bronchial asthma, cardiac and renal dyspnoea, etc.

[P1 87] **Pitalin** (*Paines & Byrne, London*). Ampoules of 1 ml. contain 5 units of pituitary (posterior lobe) extract and 0.5 mg. of adrenaline. Dose—1 ampoule repeated as necessary. Asthma

[P1 87] **Piton** (*Organon Laboratories, London*). Brand of pituitary (posterior lobe) extract containing 5 units in 1 ml., with 0.0005 g. of adrenaline

[P1 87] **Pituchinol** (*Homburg Pharma, London*). Pituitary (posterior lobe) extract and quinine base. Ampoules contain 1 ml. = 3 units of pituitary extract and 1 g. of quinine. Stimulating and regularising uterine contractions in all stages of labour

[P1 87] **Thymuitrin** (*Richter, London*). Pituitary (posterior lobe) extract 10 units, thymus 5 g. Dose—0.5 to 1 ml. intramuscularly when indicated. Uterine inertia and during first stage of labour

[P1 87] **Uterothym** (*Richter, London*). Uteritin (see p. 779) 5 units and thymus 2 g. Dose—0.5 to 2 ml. intramuscularly. Induction of labour, uterine inertia.

### Active Principles of the Posterior Lobe

Sir H. H. Dale and others have shown that the actions on the uterus and on the blood pressure are due to different substances, and the two active principles have been separated from pituitary (posterior lobe) extract. These are referred to as the *oxytocic* principle and the *pressor* principle of the pituitary (posterior lobe).

Separation of the oxytocic and pressor principles of the posterior lobe (termed  $\alpha$  and  $\beta$  hypophamine respectively) as stable water-soluble powders. Fresh posterior lobes from ox pituitaries, desiccated with acetone, are extracted with 0.25% acetic acid and concentrated at low temperature. The solution is salted out with sodium chloride or ammonium sulphate, and the precipitate, which contains the active principles, is treated with anhydrous acetic acid. This extracts the active principles but very little protein, and the extract is fractionated by successive treatment with acetone, ether and light petroleum. 50 g of fresh posterior lobe material yielded 8 g of desiccated powder, and from this 0.05 g of purified pressor principle and 0.015 g of purified oxytocic principle were obtained as white stable powders soluble in water.—O. Kamm and co-workers, *J. Amer. chem. Soc.*, 1928, 50, 573.

Separation of the active principles by fractional precipitation from alcoholic solution by ethyl acetate.—R. L. Stehle, *J. biol. Chem.*, 1933, 102, 573.

A method for separating and purifying the oxytocic and pressor constituents of the posterior lobe of the pituitary gland. The potency of the pressor preparation obtained was 100 times that of standard pituitary powder and that of the oxytocic preparation 125 times. The yield of pressor substance was considerably higher than that of the oxytocic. Both preparations appear to be polypeptides containing tyrosine, cystine (or something which gives similar colour reactions when the methods of Folin and Denis and of Sullivan are applied) and arginine, and probably other amino-acids. They do not appear to contain histidine, and the pressor substance at least does not contain phenylalanine. Tests, which are not regarded as necessarily final, seem to exclude the presence of glutamic acid, aspartic acid and leucine in the pressor substance. The oxytocic substance was not examined for these amino-acids.—R. L. Stehle and A. M. Fraser, *J. Pharmacol.*, 1935, 55, 136.

Action of oxidising and reducing agents on the oxytocic principle. Oxytocic action diminished by reduction and restored by oxidation. Presence of a disulphide linkage suggested.—J. M. Gulland and S. S. Randall, *Biochem. J.*, 1935, 391.

The action of the post-pituitary principles on the blood.—F. R. Curtis and J. W. Pickering, *Lancet*, ii/1928, 695.

Oxytocin possesses the stimulant action of pituitary whereas vasopressin has no such effect, even in large doses. Oxytocin may safely be used in labour by those who have refrained from using pituitary extract because of the danger of "pituitary shock." It has the same action as pituitary extract but is without any of its vasomotor effects.—A. W. Bourne and J. H. Burn, *Lancet*, ii/1928, 695.

Oxytocin has no anti-diuretic activity. Vasopressin (but not oxytocin) possesses the power of pituitary extract of inhibiting the hypoglycæmic effect of insulin. Oxytocin intravenously after hæmorrhage produces increased coagulability.—O. Kamm, per *Prescriber*, 1929, 183.

Both the oxytocic and pressor principles possess the property of antagonising insulin, but not to equal degrees. They also diminish the hyperglycæmic action of adrenaline.—M. R. Gurd, *Quart. J. Pharm.*, 1934, 661.

A gastric lesion produced by an extract of the pituitary gland. The posterior lobe contains a substance which, when injected subcutaneously, causes a lesion of the acid-secreting area of the stomach. It is present in the B.P. extract, which has this effect when administered by the mouth in large doses. It may be a distinct active principle, since the oxytocic principle alone does not possess this action, although the pressor substance does.—E. C. Dodds, R. L. Noble and E. R. Smith, *Lancet*, ii/1934, 918.

Evidence is offered that mild insulin hypoglycæmia in dogs can be completely abolished by small doses of oxytocic hormone of the posterior lobe of the pituitary; corresponding doses of the pressor fraction have little or no effect. Larger doses of the oxytocic hormone not only abolish the insulin effect, but cause a rise in the blood-sugar level above normal.—H. C. Ellsworth, *J. Pharmacol.*, 1936, 56, 420.

Blood pressures and intestinal actions of pituitary (posterior lobe) extract, injected intravenously in the unanæsthetised dog, vary markedly with the fraction used, even when equal pressor-assayed dosages are employed. The presence of the oxytocic hormone may inhibit or abolish the typical effects of the pressor constituent. It is thus concluded that the pressor hormone *per se* causes, under such conditions, a fall of blood pressure, stimulation of intestinal activity, and defecation, while the oxytocic constituent *per se* in sufficient dosage exerts a definite antagonistic influence in respect of these actions. These observations may explain some of the conflicting reports on the clinical usefulness of the agents in question—K I. Melville, *J. Amer. med. Ass.*, 1/1936, 105

[P 87] **Pitocin** (*Parke, Davis, London*), formerly termed oxytocin, and [P 87] **Uteritin** (*Richter, London*) are solutions of the oxytocic principle containing 10 oxytocic units per ml.

[P 87] **Pitressin** (*Parke, Davis, London*), formerly known as vasopressin, a solution of the pressor principle containing 20 pressor units per ml. 1 pressor unit is the pressor activity exhibited by 0.5 mg of international standard pituitary (posterior lobe) powder

**Used** for the treatment and prevention of surgical shock, for the control of diabetes insipidus, and for cases of post-operative intestinal distension.

Doses of 1 ml. of Pitressin intramuscularly, repeated every 4 hours up to 8 or 12 doses, the first dose being given directly following operation, recommended for the prevention of post-operative intestinal distension in abdominal operations—Potter and Mueller, *Ann. Surg.*, 1932, 94, 364

Pitressin found more effective than the use of enemas for elimination of confusing gas shadows during cholecystography. Report of 73 cases—Collins and Root, *J. Amer. med. Ass.*, 11/1936, 32

**Intermedin.** The hormone of the *pars intermedia* which acts on the chromatophores of cold-blooded animals—B Zondek, *J. Amer. med. Ass.*, 1/1935, 637

### Anterior Lobe

[P 87] **Pituitary (Anterior Lobe) Extract.** *Prop. Names.* ANT-OXYLIN (*Oxo, London*), ANTUITRIN (*Parke, Davis, London*), PITEXAN (capsules for oral use) (*Paines & Byrne, London*), PRÆPHYSON (*Promonta, Hamburg; Pharmaceutical Products, London*).

Extracts of this part of the pituitary body prepared by different methods exhibit a number of different physiological effects, and the presence in the gland of five, and possibly more, different principles has been postulated. It is still open to doubt whether these are all separate hormones and, in fact, none of them has yet been prepared in an absolutely pure state.

Increased secretion by the anterior lobe before completion of growth produces gigantism, but if growth is completed before this hypersecretion the result is acromegaly. There is also a relationship between the anterior lobe and the gonads. Overgrowth of the lobe is associated with changes in the sexual glands; undergrowth results in infantilism. A general underfunctioning of the anterior lobe is considered to be the cause of Simmonds' disease characterised by signs of premature senility.

In addition to the factors which influence growth and the development of the gonads, the anterior lobe of the pituitary



appears to contain principles which act on the thyroid gland, the mammary glands, the pancreas and the adrenal glands. The *growth hormone* may be extracted together with other substances from anterior lobe tissue by the use of dilute aqueous alkali; from this solution it may be precipitated by acetone, extracted from the precipitate with acetic acid (95 to 98%) and further purified. An alternative method is to acidify the alkaline extract, filter, and add to the filtrate ammonia to 1% concentration, then calcium chloride and sodium phosphate, the precipitate of calcium phosphate carries down the active principle. From the precipitate it is extracted with very dilute alkali, the pH adjusted to 6.5, made alkaline with ammonia and concentrated *in vacuo* to pH 7.5 to 8. A semi-crystalline mass separates, representing 0.1 to 0.2% of the original material (see Collip, Selye and Thomson, *Proc. Soc. exp. Biol., N.Y.*, 11/1933, 544, 588, 913). Collip gives the name "Q-extract" to a substance prepared in this way. It is said to be free from the thyrotropic and gonadotropic principles, and to cause maximum growth response in test animals when as little as 1 mg. is injected daily.

[P1 87] **Phyone** ( $\phi\nu\omega$ , I cause to grow) *Prop. Names* ANTUITRIN "GROWTH" (Parke, Davis, London), KRESCONE (Paines & Byrne, London)

The growth-promoting substance from the *pars glandularis* of the hypophysis

A method of preparing a potent, non-irritating phyone extract suitable for clinical use —H B Van Dyke and Z. Wallen-Lawrence, *J. Pharmacol.*, Dec., 1930, 413

Treatment of endocrine dwarfism with growth hormone from the anterior pituitary gland.—W Englebach and R L Schaefer, *Endocrinology*, 1934, 18, 387

The growth hormone of the anterior pituitary —H M. Evans, *J. Amer. med. Ass.*, 1/1935, 1232

Growth factor of the anterior hypophysis —*Lancet*, 1/1935, 505

### **The Gonadotropic Factors.**

Extraction of anterior pituitary glands with acid or alkali, aqueous pyridine or aqueous butyl alcohol, yields a solution which when injected into young rats or mice has a stimulating action on the development of the gonads. In the female it causes development of the Graafian follicles and formation of corpora lutea.

Zondek considers the sex-stimulating autocoid to be of a dual nature, one portion influencing the ripening of the follicle and the other the formation of the corpus luteum, termed respectively *Prolan A* and *Prolan B* —*Per Prescriber*, 1931, 195

F. A. Crew and B P Wiesner name the sex-factors *Rho-one* and *Rho-two* —*Brit. med. J.*, 1/1930, 777

The principle is soluble in water, acid and alkali, is apparently more resistant to acid than to alkali and is moderately resistant to heat, although boiling purified preparations in slightly acid solution destroys it. It does not dialyse, and is probably a protein —J. Van Dyke, *J. Pharmacol.*, 1933, 47, 163, *ibid.*, 1930, 40, 413.

Van Dyke has suggested that it be named *Hebin* —A T Cameron, *Recent Advances in Endocrinology*, 1935.

The follicle-stimulating factor is gametogenic in its action, i.e., it stimulates the male germ cells, the ova, and granulosa. The luteinising factor appears to act predominantly on the theca cells of the ovaries and the interstitial cells of the testes.

The two principles have been partially separated by extracting desiccated sheep pituitaries with aqueous pyridine. From this extract a fraction soluble in water was obtained and was very active in stimulating growth of ovarian follicles, but relatively inactive in luteinising properties. A less soluble fraction was practically inactive for follicle-stimulation but produced luteinisation.—H. L. Fevold, F. L. Hisaw and others —*Amer. J. Physiol.*, 1933, 104, 710.

Separation of the two constituents (prolan A and B) has recently been attained. In the male infant animal, prolan A is apparently without effect, but prolan B has a strong stimulant effect on the development of the penis, the descent of the testes and on the seminal vesicles —*Brit. med. J.*, 1/1935, 426.

### **Gonadotropic Factors from Other Sources.**

The urine of women after the menopause, or after surgical removal of the ovaries, contains a substance that is follicle-stimulating in action but without luteinising effect. This follicle-stimulating factor may result from increased secretory activity of the anterior pituitary due to removal of the inhibitory influence of hormones produced by the ovary. The urine of pregnant women contains a substance which, although not entirely free from follicle-stimulating action, is mainly luteinising in effect.

The source of the gonadotropic hormone in pregnancy urine is a matter of dispute, but most of the evidence suggests it is formed in the chorionic tissue of the placenta. Much of the clinical work with gonadotropic hormones has been done with extracts prepared from pregnancy urine termed anterior-pituitary-like (A.P.L.) hormones.

For a method of preparation see B.P.C.

Adsorption on charcoal at pH 4 and extraction with N/10 NaOH at pH 12 to 13, yields a concentrated preparation which does not give the biuret or Millon tests —C. A. Elden, *J. biol. Chem.*, 1933, 101, 1.

ABORTION.—In habitual abortion, 100 rat units twice weekly from second to fifth month of pregnancy —A. Bourne, *Practitioner*, 11/1933, also L. Williams, *Lancet*, 11/1935, 796.

ACNE VULGARIS.—The underlying cause of acne may be a hypofunctional disturbance of the anterior lobe of the pituitary gland. Successful treatment reported with gonadotropic hormone from pregnancy urine, in doses of 2 ml. on alternate days, except that in female patients injections were omitted during the menstrual periods. Duration of treatment from a few days up to sixteen weeks —C. H. Lawrence, *J. Amer. med. Ass.*, 1/1936, 983.

CRYPTORCHIDISM.—Treatment with gonadotropic extract of anterior lobe of pituitary glands caused descent of the testes in 12 out of 17 cryptorchid boys.—Werner and co-workers, *J. Amer. med. Ass.*, 1/1936, 1541.

Six injections of Pregnyl to enlarge the testis are recommended before operation and 12 injections to prevent atrophy after operation —E. McLellan, *Lancet*, 1/1936, 999.

Spontaneous descent occurs by the seventeenth year in 87% of cases, and treatment with gonadotropic hormone should be withheld until after the age of 16 —P. Williams, *Lancet*, 1/1936, 426.

Successful results obtained by doses of 500 rat units of hormone intramuscularly twice weekly, an account of 33 cases, period of treatment ranged from two weeks to 14½ months.—Spence and Scowen, *Lancet*, 11/1935, 1335, see also *Proc. R. Soc. Med.*, 1935, 427.

Polydipsia and polyuria with slight glycosuria followed administration of Antutrin S for bilateral undescended testes but disappeared when treatment was discontinued. Both testes remained undescended —H. Koplin, *J. Amer. med. Ass.*, 1/1936, 374.

DIABETES INSIPIDUS in a patient with undescended testes apparently cured by gonadotropic hormone from pregnancy urine. After 25 doses of 100 rat units there was complete descent of testes and cure of diabetes insipidus.—Allen and Stokes, *J. Amer. med. Ass.*, 1/1936, 780.

**STERILITY.**—Two cases of sterility in males in which spermatogenesis followed administration of gonadotropic hormone from pregnancy urine *Dose*.—100 rat units weekly.—V. E. Lloyd, *Lancet*, 1/1936, 474.

**Antuitrin "S"** (Parke, Davis, London). Solution of the anterior-pituitary-like hormone from pregnancy urine containing 100 rat units per ml *Dose*.—0.5 to 2 ml twice or thrice weekly. Sterility, menorrhagia, clunacteric hæmorrhage, habitual abortion, cryptorchidism, aspermia, etc

[P1 87] **Glanduantin** (Richter, London). Anterior pituitary hormone in dry ampoules. For intramuscular injection in sexual hypofunction, amenorrhœa, etc

**Gonadotraphon** (Paines & Byrne, London). Follicle-maturing hormone and the luteinising hormone. In impotence, sterility, menorrhagia, metrorrhagia, dysmenorrhœa due to uterine hypermotility, habitual and threatened abortion. Supplied in tablets containing 100 and 200 rat units, and in ampoules containing 100 units

**Pregnyl** (Organon Laboratories, London) Anterior pituitary-like gonadotropic hormone from the urine of pregnant women Tablets contain 90 rat units, and ampoules for injection 30 or 100 rat units In women for hypermenorrhœa, dysmenorrhœa, abortion In men for cryptorchidism and azoospermia

[P1 87] **Prolan** (Bayer Products, London) Standardised anterior pituitary hormone *Dose*.—Intramuscularly 100 to 300 units daily, or *per os* 2 to 3 pellets (300 to 450 units) daily. Ovarian hypofunction

### **The Thyrotropic Principle.**

The relationship of the anterior pituitary and thyroid function is discussed under Thyroideum, p. 891.

Probably the purest preparation yet available is that of Anderson and Collip (*Proc. Soc. exp. Biol.*, N.Y., 1933, 30, 680).

The filtrate and washings from the calcium phosphate precipitate formed during the preparation of the growth factor (*vide antea*) are repeatedly precipitated with ammonium sulphate and the precipitate dissolved in alcohol or acetone until finally a pure white protein-like substance is obtained This may contain traces of the adrenotropic principle but the growth-promoting factor is absent The product is readily soluble in water and in dilute acids and alkalis, insoluble in lipid solvents, soluble in aqueous alcohol, ether and pyridine It is stable in powder form, but decomposes in aqueous solution—A. T. Cameron, *Recent Advances in Endocrinology*, 1936

### **The Lactogenic Principle** (Prolactin or Galactin).

By isoelectric precipitation of an extract of anterior pituitary tissue a fraction was obtained which stimulates development of the crop-gland in pigeons. Salt-free preparations at pH 8 can be boiled for 1 hour with little loss of potency. It is stable in solution in the presence of trisresol and completely soluble at pH 8—O. Riddle, *J. Amer. med. Ass.*, 1/1935, 636.

The preparation of prolactin by extraction with 60 to 70% ethyl alcohol at pH 9 to 10 and subsequent precipitation at pH 6.0—R. W. Bates and O. Riddle, *J. Pharmacol.*, 1935, 55, 365.

Preparation of galactin by extraction of acetone-dried powder with glacial acetic acid.—McShang Turner, *Proc. Soc. exp. Biol.*, N.Y., 1935, 52, 1655

This factor seems to be under control of the œstrogenic hormone during pregnancy. At parturition, with loss of the placenta, the level of œstrogenic substance drops sharply, permitting the release of the lactogenic factor of the pituitary

Prolactin has been tried clinically with reported success in women whose supply of milk had failed.—*Prescriber*, 1936, 184

The clinical use of prolactin—*Endocrinology*, 1934, 18, 18

### **Relation to the Pancreas.**

The relationship between the anterior pituitary and the pancreas may have an important bearing on diabetes. A diabetogenic

factor, a ketogenic factor and a pancreatropic factor have all been recognised, but it is uncertain whether or not these are separate principles.

The diabetogenic factor is concerned with carbohydrate metabolism, the ketogenic factor with fat metabolism, and the pancreatropic with the secretion of insulin by the islets of Langerhans—*See Prescriber*, 1936, 182.

The blood plasma of elderly obese patients with glycosuria contains a substance antagonistic to insulin and similar in this action to extracts of anterior lobe of the pituitary—De Wesselow and Griffiths, *Lancet*, 1/1936, 991.

### ***The Adrenotropic Principle or Interrenotropic Principle.***

After removal of the pituitary from rats the adrenal cortex atrophies and this change can be prevented or the normal condition restored by intramuscular grafting of fresh rat pituitaries. An extract containing this adrenotropic principle can be prepared from the alcoholic mother liquors from which most of the thyrotropic principle has been removed (*vide antea*). The fraction soluble in 75% alcohol yields on concentration in the aqueous phase at pH 5 to 6 a flocculent precipitate which is extracted with dilute ammonia. The ammonia is removed by distillation *in vacuo*; the residue does not contain the thyrotropic, gonadotropic or growth factors but restores the atrophied adrenal cortex of rats after removal of the pituitary to normal in doses of 0.25 mg per day.—J. B. Collip, E. M. Anderson and D. L. Thomson, *Lancet*, 11/1933, 347.

(For details of biological tests for the anterior pituitary factors see Vol. II.)

### **Dried Pituitary Preparations.**

Of these there are three, made respectively from the *Entire Gland*, the *Anterior Lobe* and the *Posterior Lobe*

[P1 87] **Pituitary Body, Dried** (*entire gland*) of the ox

*Dose*.—1 to 3 grains (0.06 to 0.2 g.) thrice daily

Five parts of fresh gland yield about 1 of dried gland

**Uses** Has been employed to improve metabolism, to raise arterial tension, to increase diuretic action and to improve appetite. Given in menstrual disorders and in exophthalmic goitre and with thyroid (*qv*) in obesity.

Small doses, e.g., 1 grain of desiccated gland, are thought to be practically useless in most cases. 5 to 10 grains thrice daily may be regarded as a minimal dose. Very large doses, e.g., 100 grains thrice daily, have been given without any apparent ill effects

*F.E. VIII* has a preparation of this kind. 1 = 4 of fresh gland.

[P1 87] **Pituitary (Anterior Lobe) Substance, Dried.**

*Dose*.—1 to 4 grains (0.06 to 0.25 g.). Much larger doses, up to 60 gr. (4 g.), are often given. 5 parts of fresh substance yield 1 part of dried substance.

**Uses.** Has been thought to exercise a stimulating action upon growth, but for this purpose it should be replaced by standardised extracts of growth hormone. The anterior lobe has been

given in certain types of obesity, also in later stages of acromegaly but not earlier stages; also in bronchial asthma

INFANTILISM and certain types of amenorrhœa associated with minor degrees of infantilism treated with anterior lobe by the mouth.—H Gardiner Hill and J. F. Smith, *Lancet*, 11/1926, 222

Extracts of the anterior lobe of pituitary gland, of the ovary, and of the mammary gland, are likely to have no therapeutic action when given by the mouth.—J. H. Burn, *Pharm J*, 1/1927, 356

**[P1 87] Pituitary (Posterior Lobe) Substance, Dried.**

*Syn.* PITUITARIUM POSTERIUM (U.S.P. XI).

*Dose.*—1 to 4 grains (0.06 to 0.25 g.) U.S.P. X average dose  $\frac{1}{2}$  grain No dose is given in U.S.P. XI 4.5 parts of the fresh substance yield about 1 of dried substance

*Uses.* Has been used in exophthalmic goitre, acromegaly and by its action on the circulatory system, to relieve cardiac dilatation, in intestinal paresis, diabetes insipidus, amenorrhœa and enuresis

DIABETES INSIPIDUS 7 cases in which nasal administration of powdered posterior lobe controlled the thirst and polyuria, with establishment of "compensation" on the second day The powder, diluted with lactose, was sniffed up the nose thrice daily, and contained 1000 Vægtlin units per gramme, the average dose being 15 to 90 units —F. Mainzer, *Brit med J Epit*, 1/1935, 72

[P1 87] **Auxanin** (*Richter, London*) [P1 87] Tablets, A thymus, thyroid and anterior pituitary—for maldevelopment and cretinism with hypogenital symptoms [P1 87] Tablets, B thymus, pineal and anterior pituitary—for maldevelopment with hypergenital symptoms

[P1 87] **Gynocalcion P** (*Anglo-French Drug Co, London*) Contains calcium, manganese and phosphorus, with pituitary extract (whole) *Dose*—4 to 5 dragées thrice daily for two periods of 8 days in the month, the first directly before and the second a few days after the monthly period In disorders of puberty.

[P1 87] **Proveinase** (*Bengue, London*) Suprarenal, pituitary, thyroid, extract of hamamelis, cupressus, horse chestnut and viburnum *Dose*—Chronic cases 2 to 3 tablets daily, acute cases 3 to 6 Phlebosclerosis, hæmorrhoids

[P1 87] **Veinotrope** (*Continental Laboratories, London*) Mixed gland tablets containing parathyroid, suprarenal, posterior pituitary, ovary or testicular extract, and plant extracts For varicose veins, hæmorrhoids, venous congestion at the menopause, etc

**Thymus Gland, Desiccated.** (1 part = 5 of fresh gland.)

A yellowish amorphous powder, prepared by desiccating the thymus glands, freed from fat, of healthy calves.

*Dose.*—B.P.C. states 2 to 4 grains (0.12 to 0.25 g.); much larger doses have been given.

Until recently the general opinion was against the inclusion of the thymus amongst the endocrine glands There is no evidence that its removal produces any appreciable result The work of Hanson (U.S.A.) indicates that extracts of thymus may contain a growth-accelerating factor. The clinical use of thymus gland is still purely empirical. The dried gland substance has been given by mouth in defective nutrition of childhood, Graves' disease, hæmophilia, anæmia, leucocythæmia, and rheumatoid arthritis, but evidence of its value in these conditions is lacking.

The absolute weight of the thymus increases rapidly during the first two years of life, changing little till the seventh year, when it again increases, to fall slightly after the eleventh year. Heavier in the male at birth and for the first four years of life, after which the weight is approximately equal in the two sexes until

the eleventh year, when it tends to be absolutely heavier in the female—A. B. Bratton, per *J Amer med. Ass*, 11/1925, 1996

**The Biological Effects of Thymus Extract.** Hanson's extract is prepared from thymus glands of 2- to 6-week-old calves by extracting with hot 0.5% hydrochloric acid 1 ml of extract equals 0.6 g of fresh calf thymus pH is about 5 Golden yellow colour, said to be very stable at room temperature—L. G. Rountree and J. H. Clarke and A. M. Hanson, *J Amer med Ass*, 11/1934, 1425.

Of late the claims of the thymus to be regarded as an endocrine structure have been discredited, but now there is a reaction Hanson's thymus extract has been shown by Rountree and others to accelerate the growth and development of rats and to increase their fertility while hastening the onset of adolescence in the offspring of rats thus treated—Sir W. Langdon-Brown, *Med Annu*, 1936, 459.

The arguments in favour of the presence of an active principle in thymus gland are (a) Hanson's extract produces acceleration in growth and development which is increased in each succeeding generation, (b) removal of thymus gland from rats results in retardation of growth and development of offspring, even in second generation, (c) this retardation is not apparent in the offspring when the parents have received injections of thymus extract

For résumé of Hanson's results, see Editorial, *Brit med J*, 1/1935, 983

The thymus gland A general review—L. G. Rountree, *J Amer med Ass*, 1935, 592

**Sol. Thymocrin** (*Endocrines Ltd, Watford*) Solution prepared from the thymus Dose—1 ml intramuscularly daily or every other day Used in psoriasis, certain dermatoses, and arthritis

### **Pineal Body.** *Syn* CONARIUM

A small reddish-grey cone-like structure, situated behind the third ventricle of the brain above the superior corpora quadrigemina. Little is known of the functions of the pineal gland, it appears to contain a substance which antagonises the action of the anterior lobe of the pituitary

Pineal extract (Hanson) in rats has retarded the rate of growth and accelerated the rate of differentiation, and has hastened the onset of adolescence in the offspring of treated parents The end result is "dwarfism" associated with sexual precocity and relative macrogenitalism The injection of succeeding generations of parent rats has resulted in the amplification of these biologic effects in their young—L. G. Rountree, J. H. Clarke, A. Steinberg and A. M. Hanson, *J Amer med Ass*, 11/1935, 373

An extract of pineal glands neutralises the growth-stimulating effect of pituitary—P. Engel, *Klin Wschr*, 1934, 15, 1248

The chief activity of the pineal is an antagonistic effect The substance having this action can be extracted in slightly alkaline aqueous solution—P. Engel, *Wien klin Wschr*, 1935, 481

## **PIX LIQUIDA**

### *B P*

*Syn.* TAR, PIX PINI (*U.S.P. XI*), PIX ABIETINARUM (*P. Helv. V*)

**Dose.**—2 to 10 grains (0.12 to 0.6 g.) in a pill with lycopodium, or in perles (2½ grains each)

Is known in commerce as Stockholm tar and is obtained by the distillation of the wood of various species of *Pinus* (*Pinaceæ*)

**Soluble** in alcohol 90%, ether, chloroform, and fixed and volatile oils.

It is useful as a diuretic and in bronchial catarrh and coughs, and has been given for gastro-intestinal catarrh

**Aqua Picis.** *Syn* AQUA PICEA, EAU DE GOUDRON.

Tar 1, sand 3, mix and add distilled water 200. Macerate with shaking for 24 hours, filter. *Dose*—5 to 10 ounces (150 to 300 ml).

**Aqua Picis** (*P Ned V*). 5% by mixing with pumice. *P. Helv. V* prepares by heating water with tar 5%, and sodium bicarbonate 3%.

**Liquor Picis Ligni.** Tar 5, powdered quillaja 10, alcohol 90% to 100

Prepare a tincture of quillaja by percolation and macerate the tar in the tincture for two days at 50° Cool, filter and make up to 100

**Pilula Picis Liquidæ.** *Dose*.—1 to 5 grains (0.06 to 0.3 g)

Tar 1, soap 1, compound tragacanth powder  $\frac{1}{2}$ , powdered liquorice  $2\frac{1}{2}$  Useful for coughs and for hæmorrhoids—best freshly made

**Syrupus Picis Liquidæ** (*B P C*)

*Dose*—1 to 2 drachms (4 to 8 ml)

Tar 0.5% w/v with alcohol 90%, sucrose and water

[P1] **Sirupus Picis cum Codeino** (*P Helv V*)

*Dose*— $\frac{1}{2}$  to 2 drachms (2 to 8 ml) Codeine 1, tar water 100, glycerin 50, alcohol 95%, 10, syrup 83.9

**Unguentum Picis Liquidæ** (*B P C.*).

Contains 70% of tar in a basis of beeswax and lard Useful for psoriasis and chronic dry eczema

**Unguentum Picis Compositum** (*P Ned V*) *Syn* RINGWORM OINTMENT

Heat together water 20, tar 16, resin 4, and add with stirring starch 16 mixed with water 30, then Venice turpentine 4, acetic acid 30% 8, and water to 100

**Unguentum Picis Pini** (*U.S.P. XI*)

Pine tar 50, yellow wax 15, petrolatum 35.

**Oleum Picis** (*B P.C.*).

*Dose*—1 to 5 minims (0.06 to 0.3 ml)

A reddish-brown empyreumatic oil obtained by the distillation of tar from various species of *Pinus*. On distillation it yields **light oil of tar** or **spirit of tar**, a colourless or pale yellow oil, free from empyreumatic odour. The residue on distillation yields rectified oil of tar (**Oleum Picis Rectificatum**), a light yellow oil, darkening on keeping and having an odour similar to that of the original oil

**Oleum Picis Rectificatum** (*U.S.P. XI*) is the volatile oil from pine tar rectified by steam distillation. *Average dose*.—3 minims.

**Syrupus Picis Pini** (*U.S.P. XI*) *Average dose*— $2\frac{1}{2}$  drachms (10 ml)

Mix rectified oil of tar 1 with water 450 and shake 15 minutes. Set aside 24 hours, filter and dissolve sugar 850 in the filtrate and make up to 1000 [P1]  $\frac{1}{4}$  to  $\frac{1}{2}$  gr of apomorphine hydrochloride may also be added to each dose Useful in chronic bronchitis and winter cough

**Ether-Soluble Tar Paste** (*Martindale, London*). *Syn* E S T P. An ointment prepared by distilling tar in steam and incorporating the ether-soluble distillate in a zinc and lanolin basis. For infantile eczema, chronic eczema with lichenification, lichen simplex chronicus (Widal) and pruritus ani.

**Taroxide** (*Abbott, Montreal, Pharmaceutical Products, London*) Ether-soluble tar distillate 1.5%, powdered zinc oxide 10%, starch 25%, petrolatum 58.5%. Moist eczema

**Pix Burgundica** (*B.P.C.*). *Syn*. BURGUNDY PITCH (a misnomer, as it comes from Finland and the Black Forest)

The exudate from *Picea excelsa* (Pinaceæ), occurring as a reddish or yellowish-brown mass. Is a mild counter-irritant.

**Emplastrum Picis** (*B.P.C.*). *Syn* POOR MAN'S PLASTER. Contains about 50% of Burgundy pitch, with olibanum, colophony, yellow beeswax, olive oil and water.

**Pix Carbonis (B.P.C.)** *Syn* COAL TAR, STEINKOHLENTEFR, PIX LITHANTHRACIS (*P Helv V*), OLEUM LITHANTHRACIS, GOUDRON DE HOUILLE

The chief constituents of coal tar are benzene,  $C_6H_6$ , and its homologues, isolated by fractional distillation from the light oil (b.p. below  $170^\circ$ ), phenol, cresols and naphthalene,  $C_{10}H_8$ , from the middle (or carbolic) oil (b.p.  $170^\circ$  to  $230^\circ$ ), cresols and their homologues from the heavy oil (b.p.  $230^\circ$  to  $270^\circ$ ), anthracene,  $C_{14}H_{10}$ , from the green oil (b.p.,  $270^\circ$  to  $400^\circ$ ), the residue is pitch. The tar also contains small quantities of basic compounds such as aniline, pyridine, acridine, carbasole, etc., and sulphur compounds such as thiophene,  $C_4H_4S$

**Pix Carbonis Præparata (B.P.).**

Commercial coal tar heated at  $50^\circ$  for one hour

**Soluble** almost entirely in chloroform and benzene, partly soluble in alcohol 90%; almost insoluble in water.

**ECZEMA.**—Infantile eczema well treated by purified coal tar and zinc oxide of each 2 parts, corn starch and soft paraffin of each 16 parts —H MacCormac, *Lancet*, ii/1923, 242

In obstinate cases a tar paint crude coal tar 1 oz, collodion 1 oz, acetone 1 oz. Applied with brush, repeated every two or three days —H G Adamson, *Lancet*, i/1925, 350

**Balneum Picis Carbonis.** *Syn.* BALNEUM BITUMINIS (*L.H.*)

Solution of coal tar 8 oz, water at  $95^\circ F$ . 30 gallons

**Collyrium Picis Carbonis (B.P.C.).** Solution of coal tar 0.6% v/v

**Liquor Picis Carbonis (B.P.)**

A solution made by macerating prepared coal tar 20% and quillaia 10% in 90% alcohol or industrial methylated spirit for seven days and filtering. The quillaia enables the solution to form an emulsion with water

**Lotio Picis Carbonis Aromatica.**

Coal tar 3 oz, ether 2 oz, alcohol 90% 1 oz. Dissolve, filter and add balsam of Peru 6 dr, salicylic acid  $1\frac{1}{2}$  dr

**Lotio Picis Carbonis Alkalina (B.P.C.).** Solution of coal tar about 1 in 50, with sodium bicarbonate in water.

**Lotio Picis Carbonis et Plumbi (B.P.C.)** Solution of coal tar about 1 in 30 and strong solution of lead subacetate about 1 in 30 in water.

**Pasta Picis Carbonis (B.P.C.)** Coal tar 15 grains, compound paste of zinc oxide to 1 oz

**Pigmentum Picis Carbonis (St. T. H.)** Crude coal tar 10 g, benzene 20 g, acetone 70 g

[P1] **Unguentum Petrolei Compositum cum Acido Salicylico (St. J. H.)** Solution of coal tar 1 dr., ammoniated mercury 15 gr., salicylic acid 10 gr., hydrous wool fat 2 dr, soft paraffin to 1 oz. For psoriasis

**Unguentum Picis Carbonis (B.P.C.).**

Solution of coal tar about 6½% in yellow soft paraffin.



**[P1] Unguentum Picis Carbonis Compositum (B.P.C.).**

Solution of coal tar about 6½% and ammoniated mercury about 3% in yellow soft paraffin.

**Anthrasol** (Knoll, Ludwigshafen, Pharmaceutical Products, London) An oily non-staining tar substitute

**Endoma** (Spicer, Watford). Ointment containing two substances, "one a product secured from the steam distillation of coal tar and the other a synthetic product similar to chrysarobin." In psoriasis, scaly dermatoses, etc.

**Liquor Carbonis Detergens** (Wright, Layman & Umney, London)  
A preparation of coal tar resembling *Liquor Picis Carbonis*. Used as a lotion, from 1 dr to 1 oz to a pint of distilled water, it forms a yellowish milky emulsion, or, as an ointment, *Liquor Carbonis Detergens* 1, *Unguentum Hydrargyri Nitratis* 3, *Unguentum Simplex* 4. In prurigo and chronic scaly skin diseases

The following is also useful in eczema: *Liquor Carbonis Detergens* 2, *Liquor Plumbi Subacetatis* 2, *Zinci Oxidum* 4, *Glycerinum* 4, *Aqua* 36

**Oleum Cadinum** (B.P., U.S.P. XI, P. *Helv.* V, *Fr. Cx. Supp.* 1920) *Syn.* JUNIPER TAR OIL, *OLEUM JUNIPERI PYROLIGNEUM*, *HUILE DE CADE*.

A dark reddish-brown or nearly black oily liquid obtained by the distillation of the wood of *Juniperus Oxycedrus* (Pinacæ) This oil is very variable.

**Soluble** 1 in 3 of ether, and in chloroform; partly soluble in cold alcohol 90%, almost completely in hot alcohol 90%, very slightly soluble in water.

In most cases of psoriasis a seborrhœa of the scalp will be found This is well treated with soap and water followed by a salicylic lotion, and by oil of cade 1 in 5 of olive oil, gradually increasing the strength till the pure oil is used.

**Oleum Cadini Aceticum.**

Acetic acid 1, cade oil 10 This and the oil itself are used for alopecia.

The following are used in psoriasis and dry eczema

**Unguentum Olei Cadini (B.P.C.).**

Oil of cade 25% in beeswax and yellow soft paraffin

**Unguentum Olei Cadini et Sulphuris.**

Oil of cade 10, sulphur 1, soft paraffin 15, hydrous wool fat 15

**Ung. Sedativ. (N.I.F.).** Calamine 55 gr, zinc oxide 55 gr, oil of cade 14 gr, hydrous wool fat ½ oz, yellow soft paraffin to 1 oz

**Oleum Fagi Pyroligneum.** *Syn.* OIL OF BEECH TAR

Used on the Continent as a source of creosote

**Linimentum Picis (Lassar)**

Beech tar 4, birch tar 3, olive oil 1, alcohol (70%) 1

**Unguentum Betulæ Compositum (St. G. H.)**

Oil of cade 1 dr, resorcinol 10 gr, ichthammol 10 gr, oil of sweet birch 10 m., lard to 1 oz

**Oleum Rusci (B.P.C.).** *Syn.* BIRCH TAR OIL, *OLEUM BETULÆ ALBÆ*, *OLEUM BETULÆ PYROLIGNEUM*.

Obtained by the destructive distillation of the wood and bark of *Betula alba*, allowing the distillate to stand, and pouring off the oily upper layer from the residual tar. Occurs as a thick brownish-black liquid. To be distinguished from *Oleum Betulæ* (p. 95.)

**Unguentum Rusci Compositum (B.P.C.)**

Contains 8% of birch tar oil with resorcinol, zinc oxide and starch in a wool fat and paraffin basis. For chilblains, eczema, prurigo and psoriasis, and for irritation due to piles.

**Pix Betula** (*P Helv V*) *Syn* BIRCH TAR A yellowish-brown oil from *Betula alba* (L.)

The above oils are used instead of tar in skin affections. The odour of russia leather is due to birch tar. They are all miscible with fats, but do not blend perfectly with alcohol

**Huile de Bouleau** is obtained by distillation of *Betula alba*

**Ung. Sedresol** (*Ferris, Bristol*)

A combination of beech tar, zinc oxide and antiseptics Sedative, antiseptic and healing in eczema, psoriasis, erysipelas, shingles, erythema, seborrhœa, dermatitis, pruritus ani and vulvæ, in inflammations and eruptions of the skin, and in burns and scalds

## PLUMBUM

Pb - - 207 22.

[P1] "*Lead acetates, compounds of lead with acids from fixed oils*"

[81] "*Lead, compounds of, with acids from fixed oils*"

[83] "*Lead acetate—in substances containing less than 4 per cent of lead acetate.*"

"*Lead, compounds of,—in machine-spread plasters*"

[86] "*Lead, compounds of, with acids from fixed oils—specify proportion as the proportion of lead oxide (PbO) that the preparation would be calculated to contain on the assumption that the lead in the poison had been wholly converted into lead oxide*"

[P1] **Plumbi Acetas** (*B.P., U S P XI, P Helv V, P Dan.*).

$(\text{CH}_3\cdot\text{COO})_2\text{Pb}\cdot 3\text{H}_2\text{O} = 379.3$ . *Syn* SUGAR OF LEAD, SACCHARUM SATURNI.

*Dose.*— $\frac{1}{2}$  to 2 grains (0.03 to 0.12 g.)

Colourless crystals or masses efflorescing in warm air

**Soluble** 1 in less than 2.5 of water, 1 in 30 of alcohol 90%, 1 in 2 of glycerin

**Incompatible** with carbonates, soluble chlorides, sulphates, tannates, potassium iodide and opium preparations. The *subacetate* is incompatible with acacia mucilage

**Antidotes. In acute poisoning.** Empty stomach by emetic, then give  $\frac{1}{2}$  oz. of magnesium sulphate in water; or use stomach tube with 2 oz. of magnesium sulphate in 2 gallons of water Demulcent drinks Hot applications to abdomen, and morphine,  $\frac{1}{4}$  gr hypodermically, if necessary for pain Sodium thiosulphate, 5 ml. of 10% solution intravenously, said to be useful.

In cases recognised before the onset of convulsions, fairly large doses of calcium lactate or phosphate are useful with vitamin D to increase its absorption. In cases with convulsions, 20 to 30 ml of 8% solution of magnesium sulphate subcutaneously or 30 to 50 ml. of 50% dextrose intravenously Magnesium sulphate by mouth. Later, large doses of calcium-gluconate intramuscularly, calcium phosphate and vitamin D for 2 or 3 months Iron for the anæmia—J R. Ross and A. Brown, *Canad. publ. Hlth J.*, 1935, 26, 237

Plumbic optical neuritis due to poisoning with lead paint treated with dilute sulphuric acid and saline laxatives, hypodermic injections of pilocarpine (the latter continued for six weeks), after the first few days potassium iodide, 5 grains thrice daily for a child of 8 years.

Potassium iodide must be used with caution—sudden death may occur due to the entrance of a large amount of soluble lead salt

Lead methyl and lead tetra-ethyl, used as anti-knock additions to petrol, have partly fallen into disuse because they are so very poisonous. When inhaled or absorbed through the skin they quickly lead to convulsions and death.—Leachke

**Treatment of lead poisoning.** Constipation treated by magnesium sulphate, colic by local heat, amyl nitrite, nitroglycerin and atropine. Calcium chloride, 20 ml of 5% solution, given *very slowly* intravenously. Attempt elimination by Acid Phos Dil or Ammon Chlor.—D Hunter, *Lancet*, 11/1929, 901

Lead poisoning treated by artificial acidosis, produced by large doses of ammonium chloride and by parathyroid (Collip).—*Lancet*, 11/1929, 1106

**In chronic poisoning** some authorities consider that sodium iodide, 10 gr doses gradually increased to 50 gr, is the best agent to bring about the excretion of lead. This should be followed later, when nearly all the lead has been removed, by sodium bicarbonate, 75 gr., 4 times daily. Treatment is best carried out intermittently. Parathormone has been successfully used by Hunter and Aub. Colic treated by calcium bromide, 8 to 10 ml of 10% solution intravenously.

Lead is an extraordinary poison as regards its selective action. It acts on the nervous system. It may act on the central nervous system, but it also acts on the peripheral—hence in chronic poisoning causes peripheral neuritis. Lead may cause gout—"poor man's gout" as it is often called. Lead occurs in the urine of everybody at the present day.—Sir W. Willcox, *Med Pr.*, Nov. 12, 1930

Ocker's treatment with sodium thiosulphate (0.6 g) in industrial poisoning in the States, also the intravenous injection of calcium chloride, 15 ml of 5% solution, relieves colic.—*Brit. med J.*, 11/1926, 344

The incidence of chronic nephritis in Queensland, Australia, found to be due to the use of white lead paint on veranda railings—transferred by children from the hand to the mouth by nail-biting and thumb-sucking, and by the imbibing of rain-drops from the veranda rails. A combination of titanium white and zinc oxide suggested as a good substitute for white lead paint.—*Brit. med J.*, 11/1929, 1211.

Cumulative effect of infinitesimal doses, *e g.*, from lead in the domestic water supply. Chief symptom a strange lethargy of body and mind—usual symptoms of plumbism absent. The remedy is simple, namely, stop ingestion of lead. No medicinal treatment is necessary.—N. Porritt, *Brit. med. J.*, 11/1931, 94.

Description of case of actress suffering from chronic lead poisoning traced to use of a grease paint containing 42% of lead oxide.—Bartelman and Dukes, *Brit. med J.*, 1/1936, 528

**Abortifacient use.** Morphine and a course of Mist Alba successful. Blue lead lines on gums disappeared. Children born in each case. In one, the woman admitted taking 60 gr of lead acetate in a fortnight.—R Craik, *Brit. med. J.*, 11/1926, 908.

**Uses.** Astringent, *e g.*, in severe diarrhoea, and as a hæmostatic (of doubtful value) in gastric ulcer, it is a powerful poison. Externally for eczema, leucorrhœa, gleet, pruritus and for bruises

#### [P1] **Glycerinum Plumbi Subacetatis (B.P.C.)**

Prepared by evaporating Liquor Plumbi Subacetatis Fortis and taking up the residue in glycerin.

In chronic eczema the glycerin of lead subacetate is useful. It should first be applied diluted 1 part with about 7 of glycerin, or *better 1 with 7 of water*, and the strength gradually increased, it desiccates the eruption without producing a hard crust. Some uterine affections are well treated with the diluted glycerin

**Injectio Plumbi (L.H.) (Vaginal).**

Strong solution of lead subacetate 60 m., water to 20 oz

**Linimentum Boeckii (P. Svec. X)**

Dilute lead subacetate solution 56, talcum 18, starch 18, glycerin 8.

**Liquor Plumbi Subacetatis Dilutus (B.P.).** *Syn.* LIQUOR PLUMBI SUBACETATIS, GOULARD'S LOTION or WATER, LOTIO PLUMBI.

1 of the concentrated solution with water to 80.

For inflamed joints after injury to bruised surfaces, lead lotion (warmed) is useful. It should be used with caution to the eyes if the cornea is damaged. In gonorrhœa, compresses are used prior to injections.

[P1] **Liquor Plumbi Subacetatis Fortis** (B.P.) *Syn* GOULARD'S EXTRACT.

Prepared by digesting lead monoxide in an aqueous solution of lead acetate. Contains 19 to 21.5% w/w of Pb, and alkalinity corresponding to 10.2 to 11.6% of PbO.

**Liquor (or Lotio) Plumbi Lactatis** is 1 part of solution of lead subacetate to 9 of milk. A little eau de Cologne may be added. For nettle rash and any skin irritation.

**Lot. Picis Carb. et Plumbi** (N.F.) Solution of coal tar (methylated) 2 dr., strong solution of lead subacetate 2 dr., water to 8 oz.

[P1] **Lotio Plumbi cum Opio** (B.P.C.)

Tincture of opium 1 in 20 in dilute solution of lead subacetate.

Although used to a certain extent in this form, opium is said to be entirely devoid of peripheral anæsthetic effects and lead likewise, because the precipitation of proteins is prevented by the intervention of the epithelium.

**Lotio Plumbi Evaporans** (B.P.C.) Strong solution of lead subacetate 1 in 80 in alcohol and water.

**Lot. Plumbi Evap. Conc.** (N.F.) Strong solution of lead subacetate  $\frac{1}{2}$  oz., industrial methylated spirit 2 oz., water to 8 oz.

**Lotio Plumbi Spirituosa.** Strong solution of lead subacetate 1, glycerin 2, alcohol (90%) 4, rose water to 32. Relieves piles promptly.

[P1 S1] **Pilulæ Plumbi cum Opio** (B.P.C.) *Dose* — 1 or 2 pills.

Contain lead acetate  $1\frac{1}{2}$  gr., and powdered opium about  $\frac{1}{4}$  gr. (*exempt* [D]).

[P1 S1] **Suppositorium Plumbi cum Opio** (B.P.) *Syn* SUP-  
POSITORIUM PLUMBI COMPOSITUM

Unless otherwise stated contains 3 grains (0.2 g.) of lead acetate and 1 grain (0.06 g.) of powdered opium in oil of theobroma *q.s.* to 15 grains (*exempt* [D]).

[P1 S1] **Tabellæ Plumbi cum Opio** (B.P.C.) *Dose*. — 1 tablet

Contain in each lead acetate 3 gr. and powdered opium  $\frac{1}{2}$  gr. (*exempt* [D]).

**Unguentum Glycerini Plumbi Subacetatis** (B.P.C.)

Glycerin of lead subacetate 1 in 6, in white paraffin ointment.

[P1] **Unguentum Plumbi Acetatis** (B.P.C.)

Lead acetate 4% in white paraffin ointment.

**Unguentum Plumbi Subacetatis** (B.P.C.)

Strong solution of lead subacetate 1 in 8, in a wool fat and paraffin basis.

[P2 S1] **Plumbi Arsenas.** A white insoluble powder. Used in paste form in horticulture.

**Plumbi Carbonas** (*B.P.C.*, *P. Helv. V*) *Syn.* WHITE LEAD, CERUSSA (*P. Helv. V*, *P. Ned. V*).

Composition corresponds approximately to  $2\text{PbCO}_3, \text{Pb}(\text{OH})_2 = 775.7$

Heavy white insoluble powder, soluble in dilute acetic and nitric acids. Used as dusting powder for burns and as a 1 to 10% ointment in skin diseases

**Unguentum Plumbi Carbonatis** (*B.P.C.*). 10% in white paraffin ointment

**Paré's Ointment** (*British Drug Houses, London*) An ointment containing finely powdered lead amalgam for application to malignant ulcers

**Plumbi Iodidum** (*B.P.C.*, *P. Helv. V*)  $\text{PbI}_2 = 461.1$

Yellow crystalline powder. Used to reduce swellings. Very slightly soluble in water. 5 to 10% ointment in skin diseases

**Unguentum Plumbi Iodidum** (*B.P.C.*) 10% in benzoinated lard.

**Plumbi Monoxidum** (*B.P.*, *P. Helv. V*, *P. Dan.*)  $\text{PbO} = 223.2$ . *Syn.* PLUMBI OXIDUM, MASSICOT, LITHARGE

Yellowish-red powder or scales. To prepare lead plasters and Liquor Plumbi Subacetatis

**Minium** (*P. Belg. IV*, *P. Helv. V*)  $\text{Pb}_3\text{O}_4 = 685.7$  *Syn.* RED LEAD. Made by heating massicot

**Plumbi Nitrates.**  $\text{Pb}(\text{NO}_3)_2 = 331.2$  Colourless or opaque crystals. Soluble in water about 1 in 2. Has been used as a dusting powder for the treatment of ingrowing toenail, the scab that forms being removed next day. A little strong phenol applied first prevents formation of pus

### Lead Treatment of Malignant Disease

Malignant neoplasms appeared to be arrested by colloidal lead intravenously.—Prof. W. Blair Bell, *Lancet*, 11/1922, 1006. Lead workers are apparently immune. Lead thought to be the best agent known at the time for destroying chorionic epithelium—*Lancet*, 11/1924, 139, 1/1926, 657.

The toxic effects of lead administered intravenously, using lead acetate, colloidal lead, lead iodide, and compounds of lead with thyroiodin and hæmoglobin—Prof. Blair Bell, W. R. Williams and L. Cunningham, *Lancet*, 11/1925, 793.

The specific character of malignant neoplasia, and the action of lead on malignant growths—Prof. Blair Bell, *Lancet*, 11/1925, 1003.

Prof. Blair Bell adopted the unfruitful trophoblastic (or chorionic) hypothesis of the nature of cancer which was first put forward by J. Beard, (*Lancet*, 1/1902, 1758)—J. A. Murray, *Lancet*, 11/1925, 1142.

Intravenous injections of a colloidal suspension of lead ("M.A.") containing 0.1% of mercury and 0.1% of lead, i.e.,  $1\frac{1}{2}$  gr. of lead per 100 ml., and a similar quantity of mercury, combined with X-ray treatment, gave a decidedly beneficial effect in a case of inoperable cancer. The dose ranged from 2 to 20 ml., a total of 368 ml. of colloidal lead, containing  $5\frac{1}{2}$  gr. of lead, being given over a period of nearly two years. Minimum danger of immediate shock or toxicity—F. Coke and J. B. Cook, *Brit. med. J.*, 1/1926, 416.

15 ml. doses of a solution of not less than 0.5% of lead used with no unpleasant reaction. It is important to avoid bad colic, vomiting and poisoning due to the use of soluble salts—Frank Coke and J. B. Cook, *Brit. med. J.*, 1/1927, 818.

The connection of lead poisoning with the comparative immunity of lead workers from cancer—Prof. Blair Bell, *Brit. med. J.*, 1/1926, 432.

Debate at the Medical Soc. of London—*Brit. med. J.*, 1/1926, 568.

The fatal amount of lead is a little more than 0.2 g. when given in a single dose. Intravenous use.—Prof. Blair Bell, *Lancet*, 1/1926, 537.

A Leitch very sceptical of the whole matter. *Lancet*, 1/1926, 658

Use of colloidal lead in prevention of recurrence of malignant disease after operation is a matter so important that every case subjected to operation for cancer, whether the disease be believed to be totally eradicated or not, should be treated as if the patient still had the disease. Thirty-one cases out of 200 believed cured between Nov., 1920 and Nov., 1925—Prof. Blair Bell, *Brit. med. J.*, 1/1926, 687

LIVERPOOL CANCER RESEARCH ORGANISATION.—The lead suspension in use at Liverpool contains metal, hydroxide, and a little carbonate and is made electrically, it contains 0.5% of lead. In serum, the lead in suspension is converted to the extent of 85% into lead phosphate,  $Pb_3(PO_4)_2$ . It then may perform the function of rendering the tumour less permeable and tend towards the production of encapsulation.—W. C. M. Lewis, *Brit. med. J.*, 11/1926, 920, *Lancet*, 11/1926, 281

Plans, co-ordination of workers, etc.—Prof. Blair Bell, *Brit. med. J.*, 11/1926, 919

5 ml. of a 0.5% colloidal lead preparation is given without effect intravenously to rabbits, but colloids differ. The preparation of Prof. Lewis found safe intravenously, but slow injections desirable.—Prof. W. J. Dilling, *Brit. med. J.*, 11/1926, 924

HISTOLOGICAL CHANGES IN CANCER TISSUES UNDER LEAD.—Most human patients with malignant disease complain of pain in the region of the neoplasm within a few hours of the intravenous injection. At least 40% of the lead given intravenously to cats is deposited in the liver within two hours of injection. Details of examination of a human case 30 hours after treatment.—E. E. Glynn, *Brit. med. J.*, 11/1926, 928

Colloidal lead in sublethal doses produces profound changes in rat tumours—in a small percentage of cases leading to permanent cure. The necessary dose also induces serious, but not irreparable, changes in the liver and blood-forming organs.—F. C. Wood, *Brit. med. J.*, 11/1926, 928

**Clinical Effects of Lead in Treatment.** Dosage has been 2 doses of 20 ml. and 2 of 15 ml. when possible, at an interval of 10 days between each. Then a month's rest. At the end of this time suitable doses amounting to 10 ml. at intervals until a total of 120 ml., i.e., 0.6 g. of lead, is reached. In cases where the tumour is of slow growth give smaller doses from the first. Interesting data of cases, showing arrest of growth, etc., in 41 of 227 cases treated.—L. Cunningham, *Brit. med. J.*, 11/1926, 931

A method of preparing colloidal lead by subjecting a solution of gelatin 0.4% and glucose 0.5%, adjusted to pH 7.2 to 7.6, to the high frequency arc between lead electrodes of about 10,000 volts, the solution being kept cold. The colloid is brown-black in colour, and is not readily oxidised.—F. Bischoff and N. R. Blatherwick, *J. Pharmacol.*, May, 1927, 27

Two cases well treated in private practice—carcinoma of the breast and carcinoma of the rectum. Appreciable improvement following courses of intramuscular injections—12 ml. at weekly intervals, with small injections locally into the nodules, a total of 12 grains of lead being given in one case and 10 grains in the other. No acute toxic symptoms. The treatment does not appear to merit such wholesale condemnation and adverse criticism as it has received.—E. Talbot, *Brit. med. J.*, 11/1928, 1035

The combined action of colloidal lead and radiation caused disappearance of tumours (experimentally) in doses which, by themselves, only result in temporary retardation.—J. C. Mottram, *Brit. med. J.*, 1/1928, 132

Chemotherapy in malignant disease.—W. Blair Bell, *Lancet*, 11/1928, 164

Correct liver function necessary. Extent and interval of dosage dependent on existing damage.—L. Cunningham and M. M. Datnow, *Lancet*, 11/1929, 655

Colloidal lead preparations should be tested to be sure that they are free from toxic effects on rabbits, and that they cause only negligible fall in blood pressure. Myocardial disease a contraindication.—W. J. Dilling, *J. Pharmacol.*, April, 1929, 461

Results in 40 cases confirm Blair Bell's contention, that in a few persons with inoperable and advanced neoplasms, arrest of disease may be obtained from combined use of lead and X-rays.—L. C. Knox, *J. Amer. med. Ass.*, 1/1929, 108

65 successes out of 305 cases treated, i.e., 21.5% of successful results. No one would suggest that possession of a knife is all that is required for surgical

cure of cancer of the stomach, yet some seem to think that for lead therapy all that is required is that lead shall be pumped into the veins —W Blair Bell, *Brit. med. J.*, 1/1929, 437.

**Lead Selenium Colloid** in cancer —A. T. Todd, *Lancet*, 1/1927, 575.

Suspension of lead selenide (D4S) in a gum ghatti solution of strength lead (metal) 0.4% and selenium 0.04% used in cancer —A. L. Taylor and E. Lloyd, *Pharm. J.*, 11/1928, 542

Colloidal lead phosphate and tetra-ethyl lead appear to be the only lead compounds suitable for use intravenously in cancer. Tetra-ethyl lead emulsion is prepared by shaking 16 g. of commercial tetra-ethyl lead with a mixture made up of 150 ml. of water, 25 ml. of saturated lecithin suspension and 10 ml. of 1% sodium oleate solution. Prepare freshly and shake vigorously before use —F. Bischoff and others, *J. Pharmacol.*, Sept 1928, 109

Lead selenide hydrosol preparation by passing hydrogen selenide into a solution of lead acetate and gelatin 5% —*Brit. chem. Abstr. A*; 1928, 704

X-radiation or radium should be applied with extreme caution, if at all, in cases recently treated with colloidal lead selenide (D 4S) —A. T. Todd and H. M. Aldwinckle, *Brit. med. J.*, 11/1929, 800.

Lead selenide used intravenously at weekly intervals. The dose ranges from 1 to 5 ml. initially. Has low toxicity. A rabbit will tolerate 4 ml. per kilo. As much as 33 ml. has been given in one dose in man without adverse effects. Reactive effects—pain—thought due to protein poisoning from breakdown of cancer tissue. Explanation of action not yet proved. It is thought to be a stimulus to the defence put up against the irritation on invasion of a malignant neoplasm. Combination of radiation with selenide being worked out. An addition to treatment is calcium chloride, to prevent lead accumulating and furnish a depot for calcium assimilation. Vitamin D and thyroid as tonic and anti-infective. Liver extract to combat anæmia —A. T. Todd, *Lancet*, 11/1930, 389.

W. Blair Bell criticises Todd's lead selenide —*Lancet*, 11/1930, 550. Reply —The lead ion may only be a vehicle for the selenium —*ibid.*, 611. Reply *ibid.*, 667. Date of priority of lead selenide discussed —*ibid.*, 713

When expense of the treatment is weighed against possible good effects it seems that lead therapy is not the solution to the cancer problem —A. Soiland and co-workers, *J. Amer. med. Ass.*, 1/1929, 106

Lead selenide not curative of cancer —*Ann. Rep. med. Res. Coun.*, 1928-29, *Brit. med. J.*, 1/1930, 560

See also *Colloidal Selenium*, p. 877

**Colloidal Lead Iodide**, containing 0.2% of lead, isotomised by means of dextrose, and containing a trace of thyroid extract (less than 0.02%) and a trace of cresol as preservative, injected intravenously in inoperable carcinoma with complete absence of reaction, and with beneficial results in selected cases, e.g., growths of the solid variety or in the solid viscera, or in situations which are not vital —D. C. L. Fitzwilliams, *Brit. med. J.*, 1/1927, 758

**Colloidal Lead Phosphate** as a substitute for colloidal metallic lead was relatively non-toxic to rats and rabbits. Method of preparation given —F. Bischoff and N. R. Blatherwick, *J. Pharmacol.*, Sept., 1927, 361

## PODOPHYLLI RESINA

B P, U S.P. XI, P. Helv V, P Dan

Syn. PODOPHYLLIN.

**Dose** — $\frac{1}{4}$  to 1 grain (0.016 to 0.06 g.) as a cholagogue and aperient pill or tablet. Takes 8 to 10 hours before producing evacuation.

A yellowish powder, or in brownish-grey masses consisting of a mixture of resins obtained either from podophyllum or from Indian podophyllum

**Soluble** completely or almost completely in alcohol 90%, insoluble in cold water, partly soluble in hot water but precipitated

again on cooling, partly soluble in chloroform, ether and dilute solution of ammonia.

It is a powerful biliary purgative and may be combined with a small dose of calomel for treatment of gall-stones. It is useful in removing *ankylostoma* and other worms.

[P1 81] **Pilulæ Podophyllini, Belladonnæ et Nucis Vomicae** (B.P.C.).

*Dose*.—1 or 2 pills

Contain 1 gr of aloe and  $\frac{1}{2}$  gr. each of resin of podophyllum, dry extract of belladonna and dry extract of nux vomica.

[P1] **Pilulæ Podophyllini Compositæ** (B P C.) *Dose* —1 pill.

Contain resin of podophyllum  $\frac{1}{2}$  gr., mercurous chloride 1 gr and dry extract of belladonna  $\frac{1}{2}$  gr.

[P1] **Pilulæ Podophyllini et Quininæ** (B P C) *Syn.* POORE'S PILLS.

*Dose* —1 pill Quinine sulphate 1 gr., resin of podophyllum  $\frac{1}{2}$  gr., dry extract of belladonna  $\frac{1}{2}$  gr., aloe 1 gr. Useful "dinner pills", must be taken with food

**Tinctura Podophylli** (B P.C.).

*Dose*.—5 to 15 minims (0.3 to 1 ml).

Resin of podophyllum 3.65% in alcohol 90%

In dose of 2 to 4 drops in tea or coffee, taken night and morning, is useful in sick headache and biliousness, where the bowels and liver are sluggish in worried and overworked patients, and in chronic diarrhoea with cutting pains and high-coloured motions. Also relieves constipation with clay-coloured motions following diarrhoea of infants, 1 or 2 drops on sugar twice or three times a day

**Tinctura Podophylli Indici** (B.P. '14) is also made same strength

**Tinctura Podophylli Ammoniata** (B P C)

*Dose* —10 to 20 minims (0.6 to 1.2 ml), diluted, as a purgative and cholagogue.

Resin of podophyllum 2% w/v in aromatic spirit of ammonia Is miscible with water The sal volatile acts as a corrective

**Podophyllum** (B.P., U S P. XI). *Syn.* MAY APPIL ROOT, AMERICAN MANDRAKE, VEGETABLE MERCURY

*Dose* —2 to 10 grains (0.12 to 0.6 g.).

The dried rhizome and roots of *Podophyllum peltatum* (Berberidaceæ) from eastern U S A. and Canada Used mainly in the form of the resin of which it yields from about 2 to 8% U S.P. XI requires a minimum of 4%.

**Podophyllum Indicum** (B P).

*Dose* —2 to 10 grains (0.12 to 0.6 g.).

The dried rhizome and roots of *Podophyllum emodi* (Berberidaceæ) from the Himalayas. It yields from 6 to 12% of resin not identical with that from podophyllum.

**Collinsonia** (B P C) The rhizome of *C. canadensis* (Labiatæ), known also as stone-root or knob-root, heal-all, hardhack Has been employed in gravel and other urinary affections Is an antispasmodic in flatulent, infantile, and



biliary colic, and locally in lax conditions of the uvula, pharynx, and vocal cords *Liquid extract*, 1 in 1, *dose*—15 to 30 minims. Suppositories containing 20 to 30 grains of the powder are also used. Has also been employed in cancer of stomach and in cystitis.

**Tinctura Collinsoniæ** (*B.P.C.*) *Dose*— $\frac{1}{4}$  to 1 drachm 1 in 10.  
Has action of podophyllum but does not cause griping

## POTASSII HYDROXYQUINOLINI SULPHAS

### B.P.C.

*Syn. and Prop. Names.* OXYCHINOLINUM SULFURICUM (*P. Helv. V.*), POTASSIUM OXYQUINOLINE SULPHATE, CHINOSOL (*Chinosolfabrik, Hamburg, C. Zimmermann, London*), SUPEROL (*Superol, Beverwijk*).

Consists of a mixture of potassium sulphate and 8-hydroxyquinoline sulphate,  $(C_9H_7(OH)N)_2H_2SO_4 = 388.2$ , containing the equivalent of about 50% of 8-hydroxyquinoline. Chinisol was originally stated to be potassium-oxyquinoline sulphate, but the content of potassium in the original article of commerce does not agree with theory. Occurs as a light yellow, crystalline powder partially melting at about  $178^\circ$ , and giving a strongly acid solution.

**Soluble** in water, sparingly soluble in alcohol, insoluble in ether.

**Uses.** An antiseptic used in skin affections in 1 in 500 to 1 in 2000 solution. Is an ingredient of some perspiration deodorants and is extensively used in proprietary chemical contraceptives.

Beneficial effects in many mycoses trichophytic conditions of face, arms and wrists cured within a week by repeated applications of 1 in 2000 solution—*Brit. med. J. Erit.* 1/1927, 49.

Diphtheria carriers treated by insufflation once or twice daily with powder containing 1 to 2% in bismuth carbonate—*Per Med. Annu.*, 1931, 155.

**CONTRACEPTIVE USE.** As a few women apparently absorb sufficient quinine to cause sleeplessness and slight digestive disturbances, a suppository of Chinisol in cocoa-butter is recommended by the C.B.C. Med. Research Committee—*Lancet*, 11/1927, 42.

Chinisol in any medium is not tolerated by a considerable number of women. Its use frequently produces inflammation and discharge, whilst sterility is stated in one instance to have been caused by it. A lactic acid pessary in conjunction with an occlusive pessary found most efficient—Norman Haire, *Lancet*, 11/1927, 143. See also *ibid.*, *Lancet*, 11/1927, 256, 308 and 360.

**Bircon Tablets** (*London Rubber Company, London*) A foaming tablet said to contain Chinisol, zinc phenolsulphonate, sodium bicarbonate and other suitable antiseptics and deodorants—*Lancet*, 1/1931, 392.

**Lomolo** (*Napp, London*) Contraceptive foaming tablets of hydroxyquinoline sulphate, zinc phenolsulphonate and an effervescent base.

**Mil-San** (*Menosine Ltd., London*)

A jelly with high viscosity and low surface tension containing boric, acetic, formic, lactic and tartaric acids, aluminum acetate and potassium hydroxyquinoline sulphate in a colloid base. Supplied in single application tubes.

**Ortho-Gynol** (*Johnson & Johnson, Slough*) Boric acid, hydroxyquinoline sulphate and glycerin in a water-soluble vegetable gum base. Supplied in individual tubes, each with applicator, or in bulk tube with single applicator.

**Patentex** (*Chemische Exportgesellschaft Vauka, Frankfurt, Kaydor, London*) Jelly containing potassium hydroxyquinoline sulphate, boric acid and solution of aluminum acetotartrate.

**Semori Tablets** (*Lustpold-Werk, Munich, Medical Laboratories, London*) Foaming tablets containing hydroxyquinoline sulphate and potassium borotartarate in a mucilaginous base

**Spetonex** (*Temmler Chemical Works, Berlin, Coates & Cooper, London*) A jelly containing aluminium acetotartrate, hydroxyquinoline sulphate, alum and boric acid.

**Speton Tablets.** (*Temmler Chemical Works, Berlin, Coates & Cooper, London*). Contain sodium bicarbonate, tartaric acid, and sodium dichlorosulphamino-benzoate

**Chiniofonum** (*B.P. Add*). *Syn. and Prop. Names* PULVIS CHINIOFONI (*U.S.P. XI*), LORETIN (*Schuchardt, Gorlitz*), QUINOXYL (*Burroughs Wellcome, London*), YATREN (*Bayer Products, London*).

**Dose.**—1 to 8 grains (0.06 to 0.5 g), by rectal injection, 15 to 75 grains (1 to 5 g) *U.S.P. XI* average dose, 15 grains

Consists of a mixture of approximately 4 parts of 7-iodo-8-hydroxyquinoline-5-sulphonic acid and 1 part of sodium bicarbonate. It contains 28.2 to 29.6% of I and 18 to 22% of  $\text{NaHCO}_3$ , and occurs as a light yellow, odourless powder with a taste at first bitter, subsequently sweetish. *U.S.P. XI* describes it as a mixture of 7-iodo-8-hydroxyquinoline-5-sulphonic acid, sodium bicarbonate and sodium iodo-8-hydroxyquinoline sulphonate containing 26.5 to 28.9% of I

**Soluble** 1 in about 25 of water with effervescence, insoluble in alcohol, ether and chloroform. Aqueous solutions are decomposed by boiling

**Uses.** In acute and chronic amoebic dysentery up to 15 grains may be given 3 or 4 times daily for a week, repeated on 2 or 3 days during 2 following weeks, or a daily enema of 200 ml of 2% solution at a temperature not above 44° has been advised. In acute and the more serious chronic cases combined rectal and oral administration may be adopted

A dose 3 times daily for a week, then an interval of 8 or 10 days, and repeat—in resistant cases supplement with nightly lavage for 6 or 8 nights, repeated after 3 to 6 days' interval (during days when lavage suspended, continue treatment *per os*, giving 0.75 to 1 g daily). Lavage should be retained all night if possible. Of value in acute and good in chronic cases, where complicated with liver abscess the intestinal lesion is ameliorated but not the abscess. In amoebic dysentery with lesions high up in the intestines lavage is useless, but oral method of value.—Louis Schwartz, Paris, 1927

Yatren, by enema, acts rapidly in the acute stage, amoebæ being apparently destroyed in 4 days.—P. H. Manson-Bahr and R. M. Morris, *Lancet*, 11/1925, 544

Advances in treatment with Yatren.—P. Manson-Bahr, *Brit med J*, 11/1927, 486-490

Some favourable reports are tabulated in the *Prescriber*, 1927, 15

The action of certain alleged intestinal antiseptics (Yatren, Dimol, Kerol, Izal.) Experiments showed "no evident action whatever in any dilution employed"—L. P. Garrod, *Brit med J*, 1/1928, 367, see also under Dimol, p. 752

In mixed amoebic and bacillary types quite contraindicated *per os*—too irritant.—J. Graham Willmore, *Proc R Soc Med*, Nov, 1928, G. C. Low, *ibid*

**Neuroyatren** (*Bayer Products, London*) A combination of autolysates of *B. prodigiosus*, *Staphylococcus aureus*, and *B. pyocyaneus* with Yatren. Of value in the treatment of disseminated sclerosis. In the majority of 25 cases treated there was either amelioration of symptoms or arrest in hitherto progressive cases. A dose of 0.1 ml intravenously or 0.4 ml intramuscularly to commence with.—S. Silverman, *Brit med J*, 11/1935, 1129

**Yatren-Casein Ampoules** are made for intramuscular and in rare cases intravenous injection. "Weak" Yatren 0.025 g. plus casein 0.025 g.; "strong" Yatren 0.025 g. plus casein 0.05 g. Doses ranging from 1 to 7 ml. are used in bronchitis, acute articular rheumatism and eye affections.

**Vioform** (*Ciba, London*) is iodochlorhydroxyquinoline, proposed as a substitute for iodoform. It contains about 40% of I and about 12% of Cl. Almost insoluble in water, sparingly in alcohol, but soluble in hot glacial acetic acid.

**Enterovioform** (*Ciba, London*). Iodochlorhydroxyquinoline in 0.25 g. tablets to be taken *per os* or crushed and suspended as enema. In amoebic dysentery, 3 tablets being given daily for 10 days and repeated after a week's rest.

**AMŒBIASIS** well treated. Clinical cure (as determined by stool examinations during a follow-up period of 3 to 6 months) in 38 out of 47 unselected cases. A total dose of 15 g. orally in 2 courses of 0.75 g. daily for 10 days; with a week's rest period between, clears the stools of *E. histolytica* in the average case.—N. A. David and co-workers, *J. Amer. med. Ass.*, 1/1933, 1660.

Clinically, Vioform compares favourably with carbarsone. Untoward symptoms (which may occur with as little as 4.0 g. of the drug) are severe gastric distress, with nausea, vomiting, colicky pains, diarrhoea, excessive flatulence, with mucus and blood in the stools. When used rectally, severe local irritation results with concentrations as low as 1:500. Vioform should not be administered in retention enemata for this reason.—H. A. Anderson, *J. trop. Med. (Hyg.)*, 1935, 271.

## POTASSIUM

K = 39.10.

**Potassii Bicarbonas** (*B.P., U.S.P. XI, P. Helv. V*)  
 $\text{KHCO}_3 = 100.1.$

*Dose*.—15 to 60 grains (1 to 4 g.)

White powder or crystals soluble 1 in 4 of water, insoluble in alcohol 90%. Antacid, diuretic and uric acid solvent. It is most valuable in acute rheumatism.

[P1] **Mist. Pot. Bicarb. c. Hyosc. (N.I.F.)** Potassium bicarbonate 15 gr., potassium citrate 20 gr., liquid extract of hyoscyamus 4 m., water to  $\frac{1}{2}$  oz.

**Potassii Carbonas** (*B.P., U.S.P. XI, P. Helv. V, P. Dan.*).  
 $\text{K}_2\text{CO}_3 = 138.2.$  *Syn.* SALT OF TARTAR.

*Dose* —2 to 5 grains (0.12 to 0.3 g.)

White deliquescent powder. Soluble 4 in 3 of water, insoluble in alcohol 90%. Employed externally; internal properties similar to those of the bicarbonate. Contains about 16% of  $\text{H}_2\text{O}$ , corresponding approximately to  $\text{K}_2\text{CO}_3 \cdot \text{H}_2\text{O}$ .

**Potassii Chloras** (*B.P., U.S.P. XI, P. Helv. V*)  
 $\text{KClO}_3 = 122.55$

*Dose*.—5 to 10 grains (0.3 to 0.6 g.).

Manufactured by the electrolysis of a hot aqueous solution of potassium chloride.

A white powder or crystals with saline taste.

**Soluble** 1 in 16 of water, 1 in 2 of boiling water, 1 in 30 of glycerin, 1 in 152 of alcohol 60%, almost insoluble in alcohol 90%.

**Incompatible** with oxidisable substances, ferrous salts, sugar, nitrites, calomel, hypophosphites, vegetable powders, potassium iodide.

**Antidotes.** Empty stomach by emetic or stomach tube. Give sodium bicarbonate in water freely. Keep patient warm. Stimulants if necessary, *e.g.*, caffeine sodium benzoate, 2 gr subcutaneously. Blood transfusion.

Less toxic than potassium chloride. Average lethal dose in rats intravenously 1.5 g per kilo (chloride 0.82 g)—J. L. Ulrich and V. A. Shternov, *J. Pharmacol.*, Jan., 1929, 8.

**Uses.** Antiseptic and a powerful oxidising agent. Is useful in stomatitis, *e.g.*, in children, and in sore mouth arising from mercurial treatment. Must not be given when the kidneys are diseased.

**Collunarium Potassii Chloratis Compositum (C L T H)**

One teaspoonful of a mixture of equal parts of potassium chlorate, borax and sodium bicarbonate (Pulvis Potassii Chloratis Compositus C L T H) to be dissolved in a quarter pint ( $\frac{1}{4}$  tumbler) of tepid water. Half of the solution to be injected with a syringe along the floor of each nostril night and morning. Afterwards blow the nose freely.

**Gargarisma Chlori (B.P.C)**

A chlorinated solution obtained by dissolving in water the products of the interaction of potassium chlorate and hydrochloric acid. To be used diluted with water.

The taste is improved if made with chloroform water.

**Gargarisma Potassii Chloratis (B P C).**

Potassium chlorate 1 in 40 in water acidified with hydrochloric acid. It contains practically no free chlorine.

**Garg. Pot. Chlor. c. Phenol (N I F)** Potassium chlorate 2 dr, liquefied phenol 1 dr, trypan blue  $\frac{1}{4}$  gr, glycerin 1 oz, water to 8 oz. Dilute 1 tablespoonful with  $\frac{1}{2}$  pint of warm water.

**Tabellæ Potassii Chloratis (B P C)** contain 5 gr. (0.3 g.).

**Tabellæ Potassii Chloratis et Boracis (B P C)** contain potassium chlorate 3 gr. and borax 2 gr.

**Trochisci Potassii Chloratis (B P C)** contain 3 gr. of potassium chlorate.

**Potassii Hydroxidum (B P, U S P XI, P Helv V, P Dan)**

KOH = 56.1 Syn POTASSA CAUSTICA.

[P2] "*Potassium hydroxide.*"

[83] "*Potassium hydroxide—in substances containing less than 12% of potassium hydroxide, accumulators, batteries.*"

[86] "*Potassium hydroxide—specify proportion as the proportion of potassium monoxide ( $K_2O$ ) which the preparation would be calculated to contain on the assumption that the potassium hydroxide in the preparation had been wholly converted into potassium monoxide.*"

[87] "*Potassium hydroxide and articles containing it must be labelled "Caution. This substance is caustic."*"

Manufactured by the electrolysis of potassium chloride solution. White deliquescent sticks or cakes, containing not less than

85% of total alkali calculated as KOH. Soluble 1 in 1 of water and about 1 in 3 of alcohol 90%, very soluble in boiling dehydrated alcohol

**Incompatibles.** Acids, metallic salts and alkaloidal salts.

**Antidotes.** Treat as for poisoning by ammonia, *see* p 170

**Uses.** Caustic for nævi and warts. Given occasionally in mixtures as *Liquor Potassii Hydroxidi*, as an antacid

**Liquor Potassii Hydroxidi (B P.)** 5% w/v.

**Dose.**—10 to 30 minims (0.6 to 2 ml), freely diluted

*Liquor Potassæ per os* caused remarkable improvement in cases of inoperable malignant disease—D M Gall, *Lancet*, 1/1924, 1104

**Liquor Alkalinus, Brandish.**

Prepared from quicklime, pearl ashes and wood ashes to contain about 5% of KOH. Was formerly used in scrofula

[P2] **Pasta Potassæ et Calcis.** *Syn* VIENNA PASTE Potassium hydroxide 5, slaked lime 6, made into a paste when required for use, with alcohol or glycerin. Used as an escharotic.

[P2] **Pasta Londinensis** is similar, using sodium hydroxide

**REMOVAL OF TONSILS** "London Paste," freshly made from the powder with a little alcohol useful. About 8 weekly applications sufficient—H Norman Barnett, *Lancet*, 1/1929, 872

**Potassii Nitris.**  $\text{KNO}_2 = 85.10$ .

**Dose.**— $\frac{1}{4}$  to  $1\frac{1}{2}$  grains (0.016 to 0.1 g)

**Antidotes.** Treat as for poisoning by amyl nitrite, *see* p 151

A crystalline deliquescent powder. It is a vasodilator, improves the cerebral circulation, and is given for migraine, asthma and epilepsy

**Pulvis Potassii Nitritus Compositus.**

Potassium nitrite  $\frac{1}{2}$  gr, potassium nitrate 18 gr, and potassium bicarbonate 25 gr, mix and dispense in parchment paper. This dose may be given every morning in a tumbler of water to reduce blood pressure, is diuretic. Has thus checked recurrent epistaxis. Should be tried for gout

**Pulvis Sodii Nitritus Compositus.**—Brunton

Sodium nitrite  $\frac{1}{2}$  to 2 gr, potassium nitrate 10 to 20 gr, and sometimes potassium bicarbonate 10 gr—in a tumbler of water every morning to reduce blood pressure. May be taken for years

**Potassa Sulphurata (B P, U S P XI, P Helv V)** *Syn* LIVER OF SULPHUR

Deliquescent masses, yellowish-brown externally, pale liver-brown internally, becoming yellowish on exposure to air, smelling of sulphuretted hydrogen. Used in skin affections

**Balneum Sulphuratum (B P C)** Contains 8 oz of sulphurated potash per 30 gallons

**Balneum Sulphuris (St M H)** contains 10 oz of sulphurated potash in 30 gallons

**Sal Aperiens Sulphuratum (B P C)** *Syn* HARROGATE SALTS

**Dose.**—1 to 2 drachms (4 to 8 g.).

Sulphurated potash 3% and potassium acid tartrate 15% in exsiccated magnesium sulphate

**Unguentum Potassæ Sulphuratæ.** Sulphurated potash 1, sodium carbonate 1, lard 8. For ringworm

**Unguentum Potassii Polysulphidi (B P C)** *Syn* DANISH OINTMENT, MARCUSSEN'S OINTMENT, LOMHOLT'S OINTMENT. Contains polysulphides of potassium equivalent to  $12\frac{1}{2}\%$  of sulphur with zinc hydroxide and benzaldehyde in a wool fat and paraffin basis. For scabies.

After cleansing, rub the ointment lightly all over the body, covering all skin, wait 15 minutes and then go to bed. Take second bath at same time next day, and wear fresh underclothing, and cure is finished. Clothes are disinfected. — Svend Lomholt, *Lancet*, 11/1920, 1251, see also *J Amer med Ass*, 11/1925, 1748.

A certain cure for scabies or itch — A. Cannon, *Brit med J*, 1/1930, 148.

**Kathiolan** (*Ferrosan*, Copenhagen, *C Zimmermann*, London). An ointment used for the same purposes as potassium polysulphide ointment.

## PYRETHRUM

(with DERRIS and STAPHISAGRIA)

**Pyrethri Flos (B P C, P Helv V)** *Syn* (DAIMATIAN) IN-SLECT FLOWERS. The dried flower heads of *Chrysanthemum cinerariæfolium* (Compositæ), containing pyrethrin I (ester of chrysanthemum monocarboxylic acid and the keto-alcohol, pyrethrolone) and pyrethrin II (the ester of the corresponding dicarboxylic acid). The B P C requires a minimum of 0.4% of pyrethrin I.

**Used** as an insecticide and insect repellant. Kerosene extracts of pyrethrum are commonly used in the preparation of fly-sprays and horticultural insecticides.

Pyrethrum can be grown in this country. Samples agreed with those from Dalmatia. The stalk contains little of the toxic principle. No difference between closed and open flowers. — F. Tutin, *Pharm J*, 11/1930, 388. Notes on chemistry and some commercial products. — *Chem & Drug*, 1/1930, 130.

**SCABIES.** Pyrethrum ointment affords an efficient agent for the treatment of scabies, it is non-irritant, cleanly, and has a pleasant odour. The ointment consists of an absorbent fatty base in which is dissolved the extractive matter of pyrethrum flowers. It contains 0.75% of pyrethrins, hence 100 g. of the ointment represents 83 g. of pyrethrum flowers. The treatment is as follows. All clothing is removed and the bedclothes changed. On the first night the patient remains in a hot bath for 20 minutes and is then soaped all over with liquid soap; he re-enters the bath, rinses off the lather, and dries himself with a rough towel. The ointment is applied over the whole body. On the second night the ointment alone is applied, but on the third the first night's procedure is repeated. In 517 cases the treatment was perfectly satisfactory in from 5 to 7 days. — S. E. Sweetzer and J. W. Tedder, per *Brit med. J Epit*, 1/1936, 36.

**DESTRUCTION OF MOSQUITOES IN AIRCRAFT.** An efficient culicide is the following solution, employed as a spray. Petrol 1000 ml, concentrated extract of pyrethrum 5 g, oil of sassafras 5 ml, methyl salicylate 20 ml. The concentrated extract is prepared by extracting powdered pyrethrum flowers with petrol-ether in a Soxhlet apparatus, the extract being then concentrated to the consistence of treacle. Oil of sassafras makes the mosquitoes come out of their hiding places and so increases the efficiency of spraying. Methyl salicylate has no action on mosquitoes, but gives the solution a definite odour. The quantity of the spray required is from 4.8 ml. per cubic metre in small spaces to 2.5 ml. per cubic metre in large spaces. — N. M. J. Jitta, per *Bull Hyg*, Jan, 1936, 43.

The increase of international travel by air has brought forth new problems in controlling the spread of quarantinable disease. With specific reference to yellow fever, the destruction of infected *Aedes ægypti* on aeroplanes while in

flight presents itself as one means of restricting the possible spread of this disease. In order to accomplish this end, however, it is necessary to have an agent which will kill these mosquitoes without hazard to human occupants of the aeroplanes. A mixture of 1 part of pyrethrum extract in kerosene (containing 2% of pyrethrins) and 4 parts of carbon tetrachloride (containing no pyrethrins) has been tried 5 ml per 1000 cubic feet, with 5 minutes' exposure, killed 100% of exposed *Aedes ægypti*. By ordinary tests this mixture is non-inflammable — C. L. Williams, *Publ Hlth Rep, Wash*, 1935, 1401

**Mosquito Larvicide.** A stable stock emulsion suitable for use as a larvicide in fresh waters and waters of less than 5% salinity is prepared by emulsifying a mixture of kerosene-pyrethrum extract (obtained by treating 2 lb. of pyrethrum flowers with 2 gal. of kerosene), 1 gal. of water and 8 oz. of 40% liquid coconut oil soap. The emulsion mixed with 10 parts of water kills mosquito larvæ but is not injurious to fish, plants or water fowl. The pyrethrum does not remain toxic after 48 hours. An emulsion suitable for use on waters of more than 5% salinity is prepared by adding a mixture of 2 oz. of cresylic acid and 2 gal. of kerosene-pyrethrum extract to a mixture of 1 lb. of powdered skim milk in 1 gal. of water. Diluted with 10 parts of water, this larvicide has no effect on goldfish and water fowl. Both larvicides are equally effective against mosquito pupæ and larvæ when used at a rate of 50 gal. or more per acre — J. M. Ginsburg, *per Trop Dis Bull*, 1936, 248.

### **Tinctura Pyrethri Floris (B.P.C.) 1 in 4**

Diluted 1 to 10 with water, it is applied to the skin to prevent insect bites

**Pymosel** (*Harwood (Chemists) Ltd, Watford*) Active principles of pyrethrum. In tablets, for oxyuria, ascariis, ankylostoma, etc., in granules for tænia

**Pyrethri Radix (B.P.C., Fr. Cx)** *Syn* PELLITORY ROOT, SPANISH PELLITORY. Dried root of *Anacyclus Pyrethrum* (Compositæ).

**Pastilli Pyrethri (B.P.C.)** contain 1 gr. (0.06 g)

For dryness of the mouth. To promote a continuous flow of saliva and thus irrigate the ducts, and so prevent ascending infection

**Tinctura Pyrethri (B.P.C.). 1 in 5** A useful sialogogue, causing considerable salivary effusion. Must be given with caution to children, as it is powerful in effect. Applied also to the gums to relieve toothache

[P1] **Tinctura Pyrethri Composita.** Tincture of pyrethrum (root) 2, clove oil 1, camphorated chloroform 1. As toothache drops.

**Derris (B.P.C.). Syn.** TUBA ROOT, AKER-TUBA.

The dried rhizome of *D. elliptica* and *D. malaccensis* (Leguminosæ), climbing plants indigenous to Malay and the East Indies. Contains up to 10% of a colourless crystalline substance, rotenone,  $C_{23}H_{22}O_6$ , together with the crystalline substances deguelin, tephrosin and toxicarol, and also a toxic substance isomeric with tephrosin. A valuable horticultural and agricultural insecticide. An insecticidal wash effective against a wide range of pests may be made from 1 lb. of powdered root, 4 oz. of soft soap with water to 1 gallon. The powder produces unpleasant symptoms when inhaled, but is probably harmless to human beings and warm-blooded animals.

**Derris Dressing for Warble Fly in Cattle.** All cattle are now required to be treated with a derris preparation for the control of the warble fly. The

dressing must be used between March 15th and 22nd, and thereafter at intervals of 27 to 32 days until June 30th. The dressing, which must be prepared immediately before use by diluting with water a preparation in powder form containing powdered derris, must contain per gallon either  $1\frac{1}{2}$  oz. of derris resins or  $\frac{1}{2}$  oz. of rotenone, and 4 oz. of soap. The soap may be added at the time of dilution or included in the powdered preparation

[P1 §1] **Staphisagria** (B.P.C.). *Syn.* STAVESACRE SEEDS.

[P1] "*Alkaloids, the following; their salts, simple or complex—Stavesacre, alkaloids of.*"

[§1] "*Alkaloids, the following; their salts, simple or complex—Stavesacre, alkaloids of, except substances containing less than 0.2% of the alkaloids of stavesacre.*"

[§3] "*Alkaloids—Stavesacre, alkaloids of,—in soaps; ointments; lotions for external use*"

[§6] "*Alkaloids—Stavesacre, alkaloids of,—specify proportion as the proportion of any one alkaloid of stavesacre that the preparation would be calculated to contain on the assumption that all the alkaloids of stavesacre in the preparation were that alkaloid*"

**Antidotes.** Give medicinal charcoal stirred up in water, then follow this with an emetic or the use of the stomach tube. Keep patient lying down and quiet.

The seeds of *Delphinium Staphisagria* (Ranunculaceæ), containing about 30% of oil and 1% of alkaloids, the most important of which is [P1 §1] **Delphinine**, dose— $\frac{1}{4}$  grain increased to  $\frac{1}{2}$  grain, soluble in water, alcohol and ether. This acts chiefly on the nervous system, first upon the bulb, next on the sympathetic. Given internally in toothache, neuralgia, earache, rheumatism, dropsy and spasmodic asthma. Locally an alcoholic solution or ointment, containing 2 to 8%, causes tingling and transient redness like veratrine. One part of the oil expressed from the seeds to 6 or 12 of perfumed olive or almond oil effectually kills pediculi of all kinds. Remove nits with a mixture of vinegar and proof spirit.

**Lotio Staphisagriæ** (B.P.C.) *Syn.* NURSERY HAIR LOTION.

A perfumed decoction of staphisagria in dilute acetic acid with alcohol, glycerin and water.

**Unguentum Staphisagriæ** (B.P.C.) A mixture of benzoined lard and yellow beeswax in which staphisagria has been digested.

## PYROGALLOL.

B.P.C., U.S.P. XI, P. Ned. V, P. Helv. V, P. Dan

$C_6H_3(OH)_3 = 126.0$ .

*Syn.* PYROGALLIC ACID

**Dose.**— $\frac{1}{2}$  to  $1\frac{1}{2}$  grains (0.03 to 0.1 g.) in aqueous solution, or in



pills with syrup—freshly prepared, and kept from the light. Very rarely given internally.

In light, small, white, odourless crystals, with m p  $129^{\circ}$  to  $135^{\circ}$ , producing a sensation of coolness on the tongue. Is obtained by heating gallic acid. It has great affinity for oxygen.

**Soluble** 1 in 2 of water, about 1 in 1 of alcohol 90% and 1 in 10 of melted lard.

**Uses.** Antiseptic in skin affections and in ringworm. Ointment 2 to 10% sometimes combined with salicylic acid 2 to 5% and ichthammol about 5%. It darkens the skin, used with silver nitrate blackens the hair. Large doses are poisonous.

Lupus vulgaris, if the area is not too large, may be treated with 40% plaster as caustic, afterwards 10% ointment is a good treatment, or apply the ointment for a long time (until blister rises), then proceed with 2% ointment, finally with a weak (0.1%) ointment.

**LUPUS VULGARIS.** Pyrogallol is the most successful caustic as it has an elective caustic effect on tuberculous granulation tissue. Best employed as soft paraffin 11, pyrogallol 3, salicylic acid 3, resorcinol 3. The ointment is smeared on a piece of lint, cut to fit the plaque to be treated, and fastened by a bandage. The dressing is changed night and morning, as much destroyed tissue as possible being removed each time. Treatment is rather painful and only tolerated for a few days at a time, when it is replaced by an indifferent soft ointment or a compress of 0.2% resorcinol solution. Valuable in dealing with the verrucose form of lupus as a preliminary to light treatment.—*Brit med J*, 11/1934, 291.

**SYPHILITIC ULCERATIONS**, resistant to usual treatment, well treated with pyrogallol ointment—2% for 2 days, 10% for 2 days, 20% for 2 days, and 30% for 8 days. The urine has to be controlled (black coloration with overdoses), undermined edges removed, and surrounding tissues protected with zinc paste.—*J Amer med Ass*, 11/1925, 314.

Fatal poisoning following treatment of a universal psoriasis with ointment containing pyrogallol. Patient collapsed 5 minutes after covering about two-thirds of body with ointment. Estimated absorption of about 10 g of pyrogallol.—*Per J Amer med Ass*, 11/1925, 555.

**Unguentum Pyrogallolis (B.P.C.)** *Syn* UNGUENTUM ACIDI PYROGALLICI 12½% in white soft paraffin

**Unguentum Pyrogallolis Compositum (B.P.C.)** *Syn* UNGUENTUM ACIDI PYROGALLICI COMPOSITUM, UNNA'S COMPOUND PYROGALLOL OINTMENT. Pyrogallol 5%, ichthammol 5%, salicylic acid 2% in yellow soft paraffin

**Acidum Pyrogallicum Oxidatum.** *Syn.* OXIDISED PYROGALLOL. A brownish insoluble powder prepared by the action of air and ammonia on pyrogallol. 3 to 10% ointment for skin affections

**Hydroquinone.**  $C_6H_4(OH)_2$  14 = 110.0 *Syn* QUINOL, HYDROCHINON. Dose—½ to 5 grains. An isomeride of resorcinol

A white powder soluble 1 in 20 of water and 1 in 4 of alcohol. It possesses stronger antiseptic and antipyretic properties than resorcinol. Is used as a photographic developer, *q.v.* Has also been suggested as an anti-oxidant, *c.g.*, in anæsthetic ether

**Eugallol** (*Knoll, Ludwigshafen, Pharmaceutical Products, London*) Pyrogallol monacetate, a yellowish syrupy liquid used either undiluted or diluted with acetone for local application in psoriasis and eczema

**Lenigallol** is pyrogallol triacetate, a white powder used with zinc paste in acute and chronic eczema

## PYROXYLINUM

*B.P., U.S.P. XI.**Syn* COLLOXILINA (*FE VIII*), COLLOXYLINUM (*P Helv V*), CELLOIDINE.

Prepared by the action of nitric and sulphuric acids on cotton. It has approximately the composition of a cellulose tetranitrate  $C_{12}H_{14}O_4(ONO_2)_4$ , and contains 11.5% to 12.3% of N. *P Helv V* describes it as a mixture of the di- and tri-nitrates.

**Soluble** freely in methyl alcohol, acetone, amyl acetate, glacial acetic acid and ether mixed with an equal volume of either ethyl or methyl alcohol.

In making gun-cotton, cellulose hexanitrate,  $C_{12}H_{14}O_4(ONO_2)_6$ , the mixture of acids contains a larger proportion of nitric acid and the time of action is longer. This body is insoluble in a mixture of alcohol and ether.

**Collodium Acetonum** (*B.P.C.*). Pyroxylin 1 in 20 with oil of clove and amyl acetate in benzene and acetone.

[P] **Collodium cum Oleo Crotonis.**

Croton oil 1 part mixed with 7 parts, more or less as required, of flexible collodion, forms a useful counter-irritant, a thin layer painted on quickly dries and its action is limited to the spot to which it is applied.

**Collodium Flexile** (*B.P.*) *Syn* COLLODION

Pyroxylin 2% with colophony and castor oil in alcohol 90% (or industrial methylated spirit) and ether. *Fr Cx* has pyroxylin 5, 95% alcohol 20, ether 75 (all by weight); *U.S.P. XI* has 4, 25 and 75, *P Dan* 4, 84 and 12, and *P. Helv V* 4, 66 and 30, respectively.

**Collodium Flexile** (*U.S.P. XI*)

Collodion with 2% of camphor and 3% of castor oil.

**Collodium Elasticum** is collodion with castor oil 5% (*Fr Cx*), 3% (*P Helv V*), 2% (*P Austr* and *P Ned V*), or 1% (*P Dan*).

**Collodium Simplex** (*B.P.C.*) Pyroxylin, about 1 in 50, in ether and alcohol 90%.

**Camphoid**, a substitute for collodion.

A solution of pyroxylin and camphor in absolute alcohol. May be used as a vehicle for the application to the skin of such drugs as iodoform, phenol, salicylic acid, resorcinol, iodine, chrysarobin and ichthammol. Iodoform dissolves in it to the extent of 1 in 10. The preparation dries in a few minutes, leaving a film which is not easily washed off.

**Celluloid.** Made by dissolving pyroxylin 50 in a solution of camphor 25 in ether 100 and manipulating the mass until it has become plastic. It is then dried. Colours may be incorporated.

It is supplied in thin sheets and, being light, rigid and washable, is useful in surgery for splinting; it is rendered plastic by rolling up and macerating in hot spirit for a few minutes; it may then be wrapped round the limb with a layer of wool outside and quickly sets. *N.B.* Very inflammable. Celluloid was originally called xylonite.

**Soluble** in acetone and in amyl acetate, but the film resulting in the first case is liable to be opaque. Mixtures of these solvents are frequently used. A collodion can be readily made strength 1 in 20 using equal parts of the solvents (The celluloid should be shredded).

**Celluloid Splints** employing **Pexuloid**, a special solution. As used at the Hospital for Sick Children, Great Ormond Street, London—Details Edn XIX, p. 361.

**"Non-inflammable"** Celluloid is cellulose acetate. It is not actually unburnable, but is as safe as paper. It burns slowly without the evolution of dangerous gases—*Lancet*, 1/1929, 1283.

Danger of inflammable films used in hospitals and by radiologists for cheapness.—*Lancet*, 11/1931, 1310.

## QUINIDINE

(with CINCHONIDINE and CINCHONINE)

**Quinidina** (B.P.C.)  $C_{20}H_{24}O_2N_2 \cdot 2H_2O = 360.2$

**Dose.**—3 to 10 grains (0.2 to 0.6 g.).

White amorphous powder or acicular crystals, m.p. when anhydrous  $168^\circ$ . It usually contains 20 to 30% of the closely related alkaloid, hydroquinidine.

**Soluble** 1 in 2200 of water, 1 in 750 of boiling water, 1 in 17 of alcohol 90%, 1 in 70 of ether. The anhydrous alkaloid is soluble 1 in 1.6 of chloroform.

Its solution in sulphuric acid has a blue fluorescence, as in the case of quinine, and it gives a similar thalleioquin reaction. It differs from quinine in m.p., and its acid tartrate and the hydroiodide are only slightly soluble.

**Uses.** Quinidine and its salts are generally considered to be as useful as quinine in malaria but are more depressant to the heart. The salts, chiefly the sulphate, are given in auricular fibrillation.

Curative effects of quinine, quinidine, and cinchonine found the same for all forms of malaria and, except for the greater cardiac depression caused by the last, no difference in toxicity.—Dale and James, *Brit. med. J.*, 11/1925, 970, see also *Spec. Rep. Ser. med. Res. Coun., Lond.*, No. 96, 1925.

These findings negative, in part, the opinions of Hugh W. Acton (*Lancet*, 1/1922, 124, 283) that all the various (14 or more) closely related alkaloids in cinchona exert a destructive action on the malarial parasite, but differ in the degree of destructive power. According to him, in benign tertian infection dextrorotatory quinidine is more efficacious than the levorotatory quinine.

**Quinidinæ Hydrochloridum** (P. Ital. V).

$C_{20}H_{24}O_2N_2 \cdot HCl \cdot H_2O = 378.7$ .

Colourless silky crystals, soluble 1 in 60 in water.

**Quinidinæ Hydrochloridum Acidum.**

$C_{20}H_{24}O_2N_2 \cdot 2HCl \cdot H_2O = 415.1$ .

Colourless crystals, soluble 1 in 4 of water.

**Quinidinæ Sulphas** (B.P., U.S.P. XI, P. Ned. V, F.E. VIII, P. Belg. IV, P. Helv. V).  $(C_{20}H_{24}O_2N_2)_2 \cdot H_2SO_4 \cdot 2H_2O = 782.5$ .

**Dose.**—3 to 10 grains (0.2 to 0.6 g.). U.S.P. XI average dose 3 grains 4 times a day.

Occurs as needle crystals, darkening on exposure to light.

**Soluble** 1 in about 90 of water, 1 in 10 of alcohol 90%.

**Uses.** In addition to its efficacy in malaria, quinidine, alone or

in combination with cinchonidine, may be tried in all forms of fever, and wherever quinine has been used, *e g*, in influenza, neuralgia, nervous headache, common catarrhs and as a general tonic

Quinidine is mainly used in the treatment of persistent auricular fibrillation, also in auricular flutter and in paroxysmal tachycardia. For auricular fibrillation, with the patient in bed, a preliminary 5 gr is given to test idiosyncrasy, following with 5 gr. 3 times daily, increasing to 30 gr per day. Administration must cease if toxic symptoms occur. When normal rhythm is obtained the daily dosage should be gradually decreased to 5 or 10 gr, which may be continued indefinitely in order to maintain permanent regularity. Fibrillation usually ceases on the third or fourth day. If no effect is produced in 10 days, the administration of quinidine is unlikely to be of any use. Toxic effects, such as headache, nausea, dizziness and skin rashes, sometimes occur. Cardiac failure and embolism have also been reported.

**AURICULAR FIBRILLATION.** In over 50% of cases quinidine restores the rhythm temporarily, but only in a much smaller number is the action permanent. When fibrillation is due to abnormal rhythm, quinidine therapy may be highly satisfactory, but when the myocardium is severely and permanently damaged, control of the ventricular rate by digitalis is of more benefit than restoration of normal rhythm. To the patient fully digitalised (by massive oral doses) 3 gr of quinidine is given, followed, if no idiosyncrasy after 12 hours, by 6 gr every 3 hours for 5 doses. When necessary, the procedure is repeated on two following days. If the normal mechanism is not then restored further treatment is not likely to give a permanent result. Quinidine tends to increase the ventricular rate, but digitalis may be given simultaneously to counteract this.—J C. Bramwell, *Lancet*, 1/1925, 1043.

In heart affections in old persons predisposed to polyuria, quinidine was found to be diuretic.—*Lancet*, 11/1926, 924.

The treatment is difficult and is best undertaken with electrocardiographic control, as toxic effects on the heart are fairly frequent. A dose of 6 gr. every 2 hours for a maximum of 5 doses to normal rhythm, then 1 gr. thrice daily for 6 to 12 weeks, first reducing the pulse frequency to between 80 and 100 while at rest in bed.—G J Langley, *Brit med J*, 1/1927, 1043.

Of 27 cases, definite and lasting benefit was obtained in 9. Having got the patient fully digitalised give a preliminary dose of 0.2 g of quinidine, 24 hours later give 0.4 g and repeat every 2 hours for 5 doses or till normal rhythm returns—if necessary another 5 doses may be given on each of the two succeeding days. When first relapse occurs give a holding dose of 0.4 g *p d* for 4 to 6 weeks, and half that dose for the next 2 or 3 months.—J C Bramwell and R. Ellis, *Lancet*, 11/1928, 966.

The after-results of treatment with quinidine have been followed in two series of patients, one first treated in 1923-8 and the other in 1929-34; almost all have been followed up to December, 1934, or until fibrillation recurred. Quinidine restored normal rhythm in 64% of 135 cases. In 34% it is still maintained after an average period of nearly 4 years. In 30% it was restored, but fibrillation recurred after an average period of two years. In 36% quinidine failed to restore normal rhythm, or did so for such a short time that it was of no practical importance. Of the earlier series, 25% still maintain normal rhythm after nine years, and 39% of the later series after two years. Quinidine is therefore an effective and often a lasting treatment for auricular fibrillation, its success depends on the careful selection of suitable patients. The ordinary patient seen in hospital is quite unsuitable, the risk is too great, and if fibrillation is arrested it generally returns too soon. Satisfactory results are obtained by paying attention to three main criteria: the absence of congestive failure, of a greatly enlarged heart, or of a long history of fibrillation.—M. Campbell and F. W. Gordon, *Quart. J. Med.*, April, 1936, 224.

For numerous earlier references to the treatment of auricular fibrillation by quinidine sulphate, see previous edition.

**HYPERTHYROIDISM** For the cardiac complications of hyperthyroidism quinine sulphate is considered superior to digitalis—*Prescriber*, 1927, 172

**MALARIA** Observations on the treatment of malaria in 1047 cases, from 1930 to 1934, in Louisiana. Treatment consisted in the administration of quinine sulphate in 2 10-grain doses for 2 days, night and morning, and 1 10-grain dose at night for 3 more days. The course is repeated only if there is a clinical relapse or the blood smear becomes positive. This course has been found effective in curing about 60% of malignant tertian and 75% tertian malaria, it relieves the acute symptoms of both quickly, is safe to use in cases of pregnancy, and may be tried in hæmaturia and in cases of quinine idiosyncrasy.—J. P. Sanders, *Amer. J. trop. Med.*, 1935, 651

**PAROXYSMAL TACHYCARDIA** Digitalis rarely appears to have any beneficial effects in paroxysmal tachycardia. Quinine sulphate is the drug of choice, but it does not uniformly give the desired results. It often diminishes the frequency and the duration of the attacks and occasionally causes their cessation. The drug must be given for long periods, and is therefore undesirable when the paroxysms occur only rarely. The dosage must be individualised, the average dose being between 16 and 20 gr daily.—F. A. Williams, *Proc. Mayo Clin.*, 1935, 763

Quinine sulphate the only therapeutic measure and successful in many cases. Dosage high— is much as 120 gr daily.—M. B. Strauss, *per Med. Annu.*, 1931, 51

**Tabellæ Quinidinæ Sulphatis** (B.P.C.) contain 3 gr (0.2 g)

**Quinicardine** (Nativelle, Paris, Wilcox, Jozeau, London) Quinine sulphate in gelatin-coated tablets containing 0.2 g

**Quinidinæ Sulphas Acidus.**  $C_{20}H_{24}O_2N_2 \cdot H_2SO_4 \cdot 4H_2O = 494.3$

Colourless crystals, soluble 1 in 8 in water.

**Cinchonidina.**  $C_{19}H_{22}ON_2 = 294.2$

In short, colourless prisms or leaflets, with m.p.  $202.5^\circ$ . Soluble about 1 in 4000 of water, and about 1 in 20 of alcohol. It does not give the thalleioquin reaction, and its solution in sulphuric acid is not fluorescent

**Cinchonidinæ Dihydrochloridum.** *Syn.* CINCHONIDINÆ HYDROCHLORIDUM ACIDUM  $C_{19}H_{22}ON_2 \cdot 2HCl = 367.1$

*Dose*—1 to 8 grains (0.06 to 0.5 g)

Crystals readily soluble in water.

**Cinchonidinæ Hydrochloridum.**

$C_{19}H_{22}ON_2 \cdot HCl \cdot H_2O = 348.7$

*Dose*.—1 to 10 grains (0.06 to 0.6 g.)

Colourless crystals, soluble 1 in 30 in water.

**Cinchonidinæ Salicylas.**  $C_{19}H_{22}ON_2 \cdot C_6H_4(OH)COOH = 432.2$  Is useful as a tonic and antiperiodic in neuralgia, rheumatism, sciatica, etc. 5 grains every 2 hours in cachets

**Cinchonidinæ Sulphas** (B.P.C.)

$(C_{19}H_{22}ON_2)_2 \cdot H_2SO_4 \cdot 7H_2O = 812.6$

*Dose*.—1 to 10 grains (0.06 to 0.6 g.)

In silky white needles from mother liquor of quinine sulphate

**Soluble** 1 in 60 of alcohol, 1 in 100 of water (more so with a little acid).

**Uses.** Has an action similar to that of quinine, but in large doses it causes epileptiform convulsions. Is considered less active than quinine in malaria. 5-gr. doses frequently repeated are of value in rheumatism and neuralgia.

**Cinchonina.**  $C_{19}H_{22}ON_2 = 294.2$

*Dose* —1 to 10 grains (0.06 to 0.6 g)

White crystals, tasteless at first, becoming bitter. Soluble 1 in 150 of alcohol 90%, and 1 in 500 of ether; almost insoluble in water (about 1 in 4000)

Cinchonine salts have a nauseous bitter taste, as prophylactics some have thought them superior to quinine. The solution in dilute sulphuric acid is not fluorescent

Idiosyncrasy to quinine. A patient had 30 gr of the dihydrochloride intramuscularly daily for 3 days, and subsequently 45 gr daily *per os*. This produced dermatitis. She could, however, take cinchonine base, 16 gr a day —W. Fletcher and E. A. O. Travers, *Brit med J*, 1/1923, 629

**Cinchoninae Dihydrochloridum.** *Syn* CINCHONINE ACID HYDROCHLORIDE  $C_{19}H_{22}ON_2 \cdot 2HCl = 367.1$

*Dose* —5 to 15 grains (0.3 to 1 g) by intramuscular injection

White crystalline powder. Soluble 1 in 0.6 of water, 1 in 6 of alcohol and 1 in 115 of chloroform. Is given by injection in malignant tertian malaria when quinine disagrees

**Cinchoninae Hydrochloridum (B.P.C.)**

$C_{19}H_{22}ON_2 \cdot HCl \cdot 2H_2O = 366.7$

*Dose* —1 to 10 grains (0.06 to 0.6 g), or more

In white acicular crystals. Soluble 1 in 20 of water and 1 in 2 of alcohol 90% and 1 in 300 of ether. Resembles cinchonidine in its action, and has been given in malaria when quinine idiosyncrasy exists. When given subcutaneously or intramuscularly is more toxic than quinine, owing to more rapid absorption

**Cinchoninae Sulphas.**  $(C_{19}H_{22}ON_2)_2 \cdot H_2SO_4 \cdot 2H_2O = 722.5$

*Dose* —1 to 10 grains or more

In hard, colourless, short rhombic prisms with a vitreous lustre. Soluble 1 in 70 of cold water, 1 in 10 of alcohol 90%

## QUININA

*B.P.C., Fr. Ch., P. Hung., P. Svec., U.S.P. XI, F.F. VIII*

$C_{20}H_{24}O_2N_2 \cdot 3H_2O = 378.3$  *P. Ned. V* is anhydrous

*Dose* —1 to 10 grains (0.06 to 0.6 g) *U.S.P. XI* average dose 15 grains

A white, minutely crystalline, flaky powder. Loses 1 molecule of water at ordinary temperatures. When anhydrous has m.p. 174°.

The amount of quinine necessary to give 20 g. to every patient suffering from malaria throughout the world has been estimated at 1,387,000 Kg. yearly. Such a demand could be met by the quinine industry. The normal sales of the 14 principal factories, excluding those of the Indian and Italian Governments, are about 500,000 Kg. yearly, and they always hold very large stocks and could rapidly increase output by 50 or 100%. Huge stocks of bark are also held and cinchona plantations are collecting only about half their possible harvest, and could greatly increase output at short notice. No world shortage of the drug exists. The difficulty is wholly economic. Even if a satisfactory synthetic substitute is found it cannot benefit mankind to the full unless it can be sold far more cheaply than the cinchona alkaloids.—*Lancet*, 1/1933, 537.

The contrast between Italy and India is striking and unflattering to the latter. The Italian Government provides its population with an adequate supply of quinine, either free (about 20 tons) or at a reduced price (about 7 tons). It has established cinchona plantations which yielded 14 tons of bark in 1927, but will yield 860 tons by 1936—more than sufficient for national requirements. India produces enough quinine to supply only one-third of its needs and the production is decreasing. The annual direct loss in India due to malaria is about £25,000,000. Only 10 million cases of malaria are treated annually out of an estimated total of 100 million. The total annual consumption is only 96 tons, against an estimated need of 680 tons. (The annual quinine output of the world is said to be about 600 tons)—*Brit. med. J.*, 1/1933, 923.

Lack of sales is not due to the price of the drug: it is due chiefly to the inability of governments to spend money on necessary arrangements for getting it to the people, and to the fact that malaria, often not being a fatal disease, the people will seldom bestir themselves to obtain quinine except when the disease is epidemic or unusually severe.—S. P. James, *Lancet*, 1/1933, 609.

**Soluble.** Slightly in water (1 in 2600), 1 in 40 of ether and about 1 in 1 of alcohol 90%, also in dilute acids, 1 in 3 of chloroform, and in aqueous ammonia. Phenazone increases its solubility in water. Its solution in dilute sulphuric acid is fluorescent, laevorotatory, and gives, with chlorine water and ammonia afterwards added, a green colour due to thalleoquin.

**Toxic Effects.** These include ringing in the ears with partial deafness, headache, giddiness, epistaxis and often skin rashes. In susceptible patients these symptoms may follow quite small doses. Very large doses result in deafness and blindness, with death from failure of the heart and respiration.

Death from 48 5-grain quinine bisulphate tablets—H. M. Raven, *Brit. med. J.*, 11/1927, 59.

Fatal poisoning in child of 2½ following ingestion of 26 5-grain tablets (sugar coated) of quinine sulphate—S. G. Willmott, *Lancet*, 11/1931, 1133.

Quinine is often used in Greece for purposes of suicide. Doses of 10 g may not give rise to serious intoxication, but doses of 20 g and more have often proved fatal—*Per Brit. med. J.*, 1/1935, 1130.

12 5-grain tablets of quinine caused giddiness, nausea, vomiting and loss of sight within 3 hours. Recovery under amyl nitrite inhalation and sodium nitrite in 2-grain doses.—H. and R. Gainsborough, *per Prescriber*, 1923, 75.

Quinine hydrochloride, 39 grains in a malaria patient, caused severe vomiting, deafness and dilatation of pupils. Total blindness for 7 weeks, after which vision was restored for 2 months, permanent blindness supervening. Possibly due to the effects of alcohol and tobacco on the nerve fibres and ganglion cells—J. S. Du Toit, *per Trop. Dis. Bull.*, 1922, 710.

The causation of quinine blindness—E. Wolff, *Lancet*, 1/1935, 1497.

**COLLAPSE.** 60 grains of quinine in hot whisky and water caused delirium and collapse. An enema of hot coffee, strychnine and digitalin hypodermically, and hot bottles, produced rapid improvement. The quinine acted as depressant to the respiratory and cardiac systems.—H. Gooch, *Brit. med. J.*, 11/1926, 115.

**DEAFNESS.** All perception of light lost and deafness, lasting for months, caused by quinine sulphate 30 grains.—F. C. Plummer, *Brit. med. J.*, 11/1925, 1062.

**URTICARIA** following quinine treatment of malaria. One case cured by injections of adrenaline and another by calcium lactate *per os*.—May T. A. Hughes, *Indian med. Gaz.*, 1926, 7.

**Uses.** Internally is a bitter stomachic useful in atonic dyspepsia and as a tonic in convalescence and debility. It was formerly used as an antipyretic in fevers, its action in reducing temperature being due to diminished heat production; it has largely been replaced for this purpose by the synthetic antipyretics. It is also

given in neuralgia, catarrh and hay-fever. Externally, a paste of quinine in a non-greasy base is of value for preventing burns due to ultraviolet radiation. Aqueous solutions of 0.5 to 1.5% of soluble salt are used in eye lotions for the treatment of corneal ulcerations, and the 1% solution is useful as a spray in hay-fever.

Pessaries containing 3 gr. of the hydrochloride in oil of theobroma basis are used as a contraceptive.

Quinine is specific in the treatment of malaria, being particularly effective against the organism when spores are being formed. It should therefore be administered about 3 hours before an attack is due, so that the concentration in the blood shall be a maximum when the spores are liberated, at which stage fever develops.

**LABOUR**—"MEDICINAL INDUCTION" (*Castor Oil and Quinine*) 2 oz of castor oil is given and an hour afterwards  $\frac{1}{2}$  oz of a mixture containing quinine sulphate 10 gr, dilute sulphuric acid 10 m, glycerin 20 m, spirit of chloroform 5 m, and water to  $\frac{1}{2}$  oz. 1 hour after, a simple enema is given. 2 hours later another dose of the mixture, also 3 hours later and again after 4 hours, the total amount of quinine given being 40 gr. Greater percentage of successes than with pituitary (posterior lobe) extract. Less danger with pituitary extract when preceded by quinine course. Quinine is definitely able to act upon a closed cervix.—K. V. Bailey, *Brit med J*, 1/1926, 18, *Lancet*, 1/1926, 282.

**EFFECT OF QUININE ON THE UTERUS** It does not excite the normal pregnant uterus and therefore will not act as abortifacient in health, but it will excite the uterus in pathological conditions and strengthen uterine contractions in labour.—*Brit med J*, 1/1923, 156.

Stimulant action of quinine in labour is very small.—A. W. Bourne and J. H. Burn, *Brit med J*, 11/1930, 87.

10 gr of quinine hydrochloride effectual in late delivery.—*Brit med J*, 1/1930, 628.

Babies born dead under quinine induction.—D. D. Ritchie, *Brit med J*, 1/1930, 414.

**QUININE IN NORMAL LABOUR** A small dose for 3 weeks prior to the date. Quinine sulphate  $1\frac{1}{2}$  gr, dilute nitrohydrochloric acid 3 m, Syrup Aurant.  $\frac{1}{2}$  dr, water to 2 dr. *Dose*—2 drachms with water thrice daily before meals. Two 8-oz. bottles will carry the patient over the 3 weeks.—D. A. Mitchell, *Brit med J*, 1/1930, 144.

By giving not more than 5 gr. a day in divided doses, commencing several weeks before the calculated date of parturition, labour is made shorter and easier, there is improved uterine tone (with no complications of irregular contraction), a definite diminution in susceptibility to infection, improvement of general health and more satisfactory puerperium.—W. M. Hewetson, *Brit med J*, 11/1933, 170. Universally good results.—D. J. Gair Johnston, *ibid*, 266. Value confirmed.—V. B. Green-Armytage, *ibid*, 397.

In a series of 100 cases, quinine given in single nightly doses of 5 gr. in the last weeks of gestation, acted as a general tonic and stimulant, and the patients felt well and were often improved. No evidence of foetal toxicity or increased foetal morbidity, and, apart from idiosyncrasy, little risk of premature labour. The effect on duration of labour is doubtful. Clinically the pains seem improved, but compared with a control series there was no significant difference. Inertia not eliminated.—F. W. Buddee, *Brit. med. J.*, 1/1934, 1159, *see also* D. A. Mitchell, *ibid*, 11/1934, 86.

The multipara with the flabby uterus must not be given any oxytocic drug. She may develop contraction ring dystocia after only 10 grains of quinine.—B. Solomons, *Lancet*, 11/1934, 11.

## References to the Oral Use of Quinine Salts in Malaria.

### Prophylactic Treatment.

Thorough treatment ranging from 5 to 10 grains on two successive days per week up to 20 grains daily, failed to prevent incidence of malaria in Salonica in 1916-17. It was estimated that at least 80 to 90% of units were infected. The prophylactic quinine was dropped in 1918, as no dose that could be tolerated



had any protective value to troops exposed under campaigning conditions — G. T. Rawnsley, *Brit. med J.*, i/1919, 501.

No general rule can be prescribed for quinine prophylaxis. It can only be decided for each individual, or body of individuals, when all circumstances relative to malaria in the particular place are known. The investigations of several workers to solve the question, "Must a man coming home from the tropics continue to take quinine?"—the answer is "Yes." A study of induced malaria — S. P. James, *Trans R Soc trop. Med Hyg.*, i/1931, 477.

As administered to troops, is issued in packets containing 4 oz. of quinine with 1½ lb. of magnesium sulphate. The mixture dissolved in 1½ gallons of water with sulphuric acid gives quinine content of 10 gr. to the oz., and is enough for 200 men. The addition of the magnesium sulphate renders the quinine unsaleable — J. F. James, *Indian med Gaz.*, Aug., 1931.

Regular quinine is, in practice, good prophylaxis against subtertian malaria. In W. Africa it has stood the test of time. It is the irregular or non-quinine taker who is continually getting malaria — O. G. Wilde, *Brit med J.*, ii/1933, 35. This view is confirmed by T. C. Louie, C. E. P. Forsyth and J. R. C. Stephens, *ibid.*, 127.

A comprehensive test was undertaken with British troops resident in highly malarious stations in the Punjab, for the purpose of reducing the harmful effect of the autumn malarial outbreaks among the men. During the three years' duration of the test there was a uniformly lower malarial rate throughout among those taking prophylactic quinine, although it was only given for two periods of 3 weeks, with an interval of 10 days between them, in doses of 10 gr. of the sulphate daily, with the exception of Saturdays, when a purge was taken — T. Young, *J. R.A.M.C.*, Aug., 1933, 90, *ibid.*, Apr., 1934, 269.

Defects of quinine as an anti-malarial are: (1) It does not prevent infection. (2) In common with all known antimalarial remedies it is not equally effective against all species and strains of the human malarial parasite. Some strains of malignant tertian malaria are not at all susceptible to quinine, but are very susceptible to Atebrin, the reverse obtains with some strains of benign tertian malaria. (3) It does not prevent relapses. Atebrin often prevents relapses in malignant tertian malaria. (4) It is quite ineffective in preventing the infection of mosquitoes which feed upon persons having malaria. Plasmoquine in doses of 0.02 g. will prevent the infection of mosquitoes with the gametocytes of malignant tertian malaria, but it does not arrest the birth and development of the gametocytes or prevent their appearance in the peripheral blood — S. P. James, *Nature, Lond.*, ii/1935, 743.

CONTROL OF QUININE THERAPY by testing the urine for the alkaloid best secured by using Tanret's acid reagent, which invariably precipitates quinine, but as it also precipitates albumin, it is necessary to ensure that the urine is albumin-free. Mayer's reagent only precipitates quinine in high dilution when the urine is acid enough — A. Neave Kingsbury, *Rep. Inst med Res F.M.S.*, 1932; *Brit med J.*, i/1934, 338.

### Curative Treatment.

The following routine treatment of malaria has given good results, the average length of treatment being 7 days —

I. *Alkaline Mixture* (Sinton) (for adult) Sodium bicarbonate 60 gr., sodium citrate 40 gr., water to 1 oz.

II. *Quinine Mixture* (Sinton) (for adult) Quinine sulphate 10 gr., citric acid 30 gr., magnesium sulphate 60 gr., water to 1 oz.

On the first day 4 doses of I and 2 of II, the latter 15 minutes after the former for next 4 days 3 doses of I followed after 15 minutes by 3 doses of II and for next 2 days 2 doses of I followed by 2 doses of II, a total amount of 180 gr. of quinine sulphate in solution being taken. — K. V. Raju, *Indian med Gaz.*, 1925, 212.

The International Health Board, U.S.A., made a vast malarial survey in one of the counties of the State of Mississippi. Over 30,000 people were examined and the conclusion was that quinine will cure all cases of malarial fever if it is given in the right doses for a sufficiently long period. Based on these results, the National Malarial Committee of the U.S. Public Health Service adopted what is known as the standard treatment for malaria in the U.S.A. In the leaflet on the Standard Treatment it is stated that, to be most effective a dose of quinine (10 gr. for a person of 15 years or older) should be taken every night before retiring, for 8 weeks without intermission. If a person is ill with acute malaria he should take the dose according to his age about

3 times each day for not less than 3 days. This will stop the fever or chills and fever. He should then take one dose every night for 8 weeks to get the malaria out of his system. Said to be 100% efficient—See also C. C. Bass, per *J. trop. Med. (Hyg.)*, 1923, 270.

In the tropics, where malignant tertian infections are much more common, most authorities recommend a daily dosage of at least 30 gr., on account of the dangers of the development of pernicious symptoms. Although in our investigations it was found that doses of less than 30 gr. daily would have a considerable curative effect, at least as far as clinical manifestations are concerned, a daily dosage of 30 gr. is considered to be the optimum, consistent with (radical) curative action and the avoidance of harm and excessive discomfort to the patient. This dose seems to be that most usually recommended for the treatment of acute attacks in the tropics, irrespective of the kind of infection. In our work the cure rate in malignant tertian malaria, treated with quinine in doses of 20 gr., was less than half that with 30 gr. doses, given over an equal period—J. A. Sinton, *Quart. Bull. Hlth. Org. L. O. N.*, 1935, 661.

Calomel and salts with large initial doses (30 to 45 gr. daily) of quinine. Malaria in Antigua—W. M. McDonald, *Brit. med. J.*, 1/1922, 597.

Give small dose of calomel (1 gr.), repeated each night. Give the quinine (hydrochloride) in 3 or 4 gr. doses, before meals and at bedtime, with 3 or 4 ounces of water. Continue for two months—T. Stone Dixon, *Brit. med. J.*, 1/1923, 1087.

Quinine in combination with arsenic in the treatment of chronic forms of malaria more efficient than quinine alone. Methylene blue used in combination with quinine in cases of quartan fever which do not react to quinine alone—R. N. Chopra, per *J. trop. Med. (Hyg.)*, 1923, 69.

Subtertian infection and benign tertian the most generally distributed—quartan the least. The first the most amenable to quinine. Begin with 15 gr. per os, increased daily to 30 gr. Neoarsphenamine given as adjuvant. Arsenic and iron injection more advisable than drenching with quinine—P. Manson-Bahr, *Brit. med. J.*, 1/1931, 23, *Lancet*, 1/1931, 843.

#### **Malaria during Pregnancy.**

Experiments showed that quinine in certain concentrations causes contraction of both the longitudinal and circular fibres of the uterus. 1 in 300,000 has no effect. 1 in 44,000 produces a tonic spasm which, if sustained, would cause asphyxia of the fetus from constrictions of the placental sinus. This concentration could only occur if the patient was nearly poisoned with quinine.

Therapeutically, as soon as malaria is diagnosed, which is a matter of urgency in pregnancy, give quinine or quinidine at once. Divide dosage into 2½ or 5 gr. doses every 2 or 4 hours—H. W. Acton, *Lancet*, 1/1921, 216.

The treatment of malaria in pregnant women—J. Dhairyam, *Indian med. Gaz.*, 1925, 165.

The emetic action of quinine is negligible during the early months of pregnancy, and in the later stages it may be combined with an opiate. Quinine treatment should be instituted in all pregnant malaria patients—Per *Prescriber*, 1928, 373.

#### **Treatment of Malarial Relapses.**

The best for old cases was a system carried out by M. Harrison in an investigation of treatment under direction of Sir Ronald Ross. It was used on 49 chronic cases, mostly of benign tertian. Only 10.2% relapsed. Fever was reduced in 12 to 24 hours, and no asexual parasites could be found after 48 hours.

Patient to remain in bed 12 days (this period may be reduced) and to receive intramuscularly in each deltoid muscle 15 gr. of dihydrochloride daily with 10 gr. of quinine hydrochloride in Mixture No. 1 (*infra*) thrice daily, totalling 60 grains of quinine daily for the 12 days. Patient is then allowed up and receives for three days Mixture No. 2 four times a day (60 gr. of quinine daily by the mouth). Patient is then put on Mixture No. 3 four times daily for 14 days (20 gr. of quinine daily). Light work allowed.

[P1 81] **Anticachexia Mixture No. 1.** For a dose after food—

Quinine hydrochloride 10 gr., tincture of ferric chloride 5 m., solution of strychnine hydrochloride 5 m., acid solution of arsenic 5 m., dilute nitrohydrochloric acid 5 m., magnesium sulphate ½ dr., syrup of tolu ½ dr., glycerin 10 m., water to 1 oz.

[P1 81] **Anticachexia Mixture No. 2.**

As No. 1, but add quinine hydrochloride 5 gr. and dilute nitrohydrochloric acid 5 m. to the dose.

**[P1 81] Anticachexia Mixture No. 3.**

As No. 1, but *reduce* the quinine hydrochloride 5 gr. and dilute nitrohydrochloric acid 5 m in each dose—*Brit. med J.*, 1/1918, 428.

In the majority of relapsing cases, quinine *per os* is adequate—20 gr either daily or twice weekly during stay in hospital. Where this is inadequate, combined oral and intramuscular administration (60 gr daily for 4 days)—E. B. Gunson and co-workers, *Lancet*, 1/1918, 866, W. Fletcher, *Lancet*, 11/1918, 432.

In "anti-relapse quinine prophylaxis" a short intensive treatment, *e.g.*, up to 180 gr. of sulphate or hydrochloride in 3 days, effects cure in a substantial proportion of cases—*Lancet*, 1/1918, 301.

For references to the use of quinine salts by injection, see the respective salts.

**Cremor Quininæ** (*B.V.H.*). Stearic acid 2 oz. (Apoth.), sodium carbonate 131 gr., liquid paraffin 144 m, quinine 240 gr., distilled water to 20 oz. (Apoth.)

**Oleinatum Quininæ** (*B.P.C.*) 25% *w/w* of quinine in oleic acid.

**Quininæ Acetylsalicylas.**

$C_{20}H_{24}O_2N_2, C_6H_4(COOH)O \cdot OC \cdot CH_3 = 504 \cdot 3$ .

*Dose.*—1 to 5 grains (0.06 to 0.3 g.).

Useful antipyretic and antiseptic compound. Contains 64.3% of quinine. *M.p.* 167°.

**Soluble** 1 in 330 of water, 1 in 50 of alcohol 90%, 1 in 7 of chloroform; insoluble in ether. Immediately decomposed by acids and alkalis.

**[P1 81] Quininæ Arsenas (*B.P.C.*)**

$(C_{20}H_{24}O_2N_2)_2, H_3AsO_4, 8H_2O = 934 \cdot 5$

*Dose.*— $\frac{1}{16}$  to  $\frac{1}{8}$  grain (0.004 to 0.008 g.)

White silky needles sparingly soluble in cold water. Contains 69% of anhydrous quinine. Owing to the small dosage possible, its action is that of arsenic.

**[P1 81] Kinectine** (*Mouneyrat, Villeneuve-la-Garenne, Anglo-French Drug Co., London*). Hectine with quinine hydrochloride (*i.e.*, benzosulphopara-amino-phenyl arsenate of quinine) *Dose.*—3 tablets a day for 3 days and then 2 tablets every other day to a total of 18 tablets. Hay fever, coryza, influenza, malaria.

**Quininæ Benzoas (*B.P.C.*)**

$C_{20}H_{24}O_2N_2, C_6H_5 \cdot COOH = 446 \cdot 3$ .

*Dose.*—1 to 5 grains (0.06 to 0.3 g.).

White crystals with alkaline reaction, containing up to 75% of anhydrous quinine. Soluble 1 in 350 of water.

**Quininæ Bisulphas (*B.P., U.S.P. XI, P. Ned. IV, P. Hung.*)**

$C_{20}H_{24}O_2N_2, H_2SO_4, 7H_2O = 548 \cdot 4$ . *Syn* QUININÆ SULPHAS ACIDUS. Termed **Neutral** in *Fr. Cx.*, *P. Ital. V* and *F.E. VIII*.

*Dose.*—1 to 10 grains (0.06 to 0.6 g.). *U.S.P. XI* average dose 15 grains. *F.E.* gives max. dose *per diem* 2 g.

Transparent or opaque needles containing about 59% of quinine.

**Soluble** 1 in 10 of water and 1 in 23 of alcohol 90%.

It is suitable for preparing eye lotions. In purulent ophthalmia, hypopyon and keratitis, drops containing 3 gr. with 12 gr. of boric acid per oz. are useful, and 3 gr. per oz. of water has a specific action on ophthalmic diphtheria. Incompatible with potassium iodide. The acid hydrochloride is best for injections. The 1 in 2000 solution may be used as an irrigation in cystitis.

**Tablets of Quinine Rhubarb Compound** contain quinine bisulphate 1 gr. jalap 1½ gr., calomel 1 gr., and rhubarb 1½ gr. Given to check malarial poisoning.

[P1-81] **Esanofele** (*Bisleri, Milan; Wilcox, Jozeau, London*). A preparation in pill form containing in each, quinine bisulphate 0.09 g., arsenious acid 0.0009 g., iron citrate 0.027 g., extract of bitter herbs 0.145 g. Used in malaria.

*Dose*—One 3 times daily for 15 days.

[P1 81] **Quininæ Cacodylas** (*B.P.C.*).

$C_{20}H_{24}O_2N_2, (CH_3)_2AsO \cdot OH = 462.2$ .

*Dose*.—*Per os* and hypodermically  $\frac{1}{4}$  to 1 grain (0.016 to 0.06 g.)  
Larger doses are sometimes given.

White acicular crystals soluble in water.

This salt has been suggested for intravenous use in malaria,  $7\frac{1}{2}$  grains (0.5 g.) in 20 ml. It has approximately the same toxicity as quinine dihydrochloride and dihydrobromide.

**Quininæ Camphoras.**  $(C_{20}H_{24}O_2N_2)_2, C_6H_{14}(COOH)_2 = 848.5$ .

*Dose*.—1 to 10 grains. An insoluble powder containing 76.4% of quinine

**Transpulmin** (*Homburg Pharma Ltd, London*) Solution of basic quinine and camphor in volatile oils. *Dose*—1 to 2 ml intramuscularly per day for from 7 to 21 days. Influenza, bronchitis, broncho-pneumonia, etc

**Quininæ Citras.**

$(C_{20}H_{24}O_2N_2)_3, C_3H_4 \cdot OH(COOH)_3, 7\frac{1}{2}H_2O = 1300$

*Dose*.—1 to 5 grains (0.06 to 0.3 g.).

**Soluble** 1 in 900. It has, therefore, little taste. Given suspended in mixture. Contains not less than 74.5% of quinine.

**Ferri et Quininæ Citras** (*B.P., P. Dan.*).

*Dose*.—5 to 15 grains (0.3 to 1 g.). 15 gr. contains about 2 gr. of iron and  $2\frac{1}{4}$  gr of quinine.

It may be given in solution, or in pills with simple syrup or mucilage of acacia (not in excess, as, unless made very hard, they lose shape). Alcohol 60% with glycerin 5% is also a suitable excipient. Greenish-yellow deliquescent scales with bitter chalybeate taste. Contains about 13% of Fe and 15% (*P. Dan.* 10%) of anhydrous quinine. Largely used as a general tonic.

**Soluble** 2 in 1 of water.

**Incompatible** with tannin and alkalis, also with phosphoric acid (ferric phosphate may be thrown out) unless considerably diluted prior to mixing

**Effervescent Citrate of Iron and Quinine.**

*Dose*—1 drachm (4 g.) = 3 grains of the salt

**Syrupus Ferri et Quininæ Citratilis.**

*Dose*.—1 drachm (4 ml.) 1 in 20 of syrup of orange.

**Vinum Ferri et Quininæ** (*B.P.C.*) *Dose*—1 to 4 drachms (4 to 16 ml.)

Contains 1 grain of iron and quinine citrate per drachm of sherry-type wine.

[P1 81] **Ferri Quininæ et Strychninæ Citras** (*q.v.*) contains 1% of strychnine.

[P1] **Sirap Neurotonique.**

*Dose*.—2 to 3 drachms (8 to 12 ml.) in a little water after meals. Iron and quinine citrate 0.50, strychnine nitrate 0.01, liquid extract of kola 5.0, sodium glycerophosphate 5.0. Dissolve with slight heat in syrup of orange, *q.s.* to 100.

**Quininæ Dihydrobromidum** (*B.P.C.*).

$C_{20}H_{24}O_2N_2, 2HBr, 3H_2O = 540.1$ .

*Syn.* QUININÆ HYDROBROMIDUM ACIDUM (*Fr. Cx.* "Neutral").

**Dose.**—1 to 10 grains (0.06 to 0.6 g.). Hypodermically, 3 to 5 grains (0.2 to 0.3 g.).

In yellowish rectangular prismatic crystals, or in powder. Contains about 60% of quinine

**Soluble** 1 in 7 of water, and is well adapted for hypodermic injection. It is non-irritating. The additional hydrobromic radical tends to prevent quinism.

**Injectio Quininae Dihydrobromidi.** 2 grains in 1 ml

**Dose** — $\frac{1}{2}$  to 1 ml

Used where quinine cannot be borne by the stomach. In malarial fever and subsequent rheumatism.

**Quininae Dihydrochloridum** (*B.P.*, *U.S.P. XI*, *P. Helv. V*).  $C_{20}H_{24}O_2N_2 \cdot 2HCl = 397.1$  *Syn.* QUININÆ HYDROCHLORIDUM ACIDUM, QUININE DI- OR BI-HYDROCHLORIDE *Fr Cx*, *P Ital. V* and *F.E. VIII* term this "neutral" quinine hydrochloride.

*N.B.*—*Fr Cx* adopted the salt +  $2\frac{1}{2}H_2O$ . Crystallised from alcohol, the salt contains alcohol and water of crystallisation. Left exposed to the air, this loses its alcohol and the salt changes to one with  $2\frac{1}{2}$  molecules of water, becoming at the same time opaque.

**Dose** —1 to 10 grains (0.06 to 0.6 g.). By intravenous and intramuscular injection, 5 to 10 grains (0.3 to 0.6 g.) *U.S.P. XI* average dose 15 grains. *F.E. VIII* has max daily dose 2 g

A white powder containing 81.6% of quinine

**Soluble** 1 in 0.6 of water, 1 in 12 of alcohol 90%

**Uses.** This is the most suitable salt for injections which have to be sterilised (*cf.* bisulphate), and it is considered the best salt for intravenous use in malaria, septicaemia, etc. Intramuscularly 20 to 30 ml. of the 10% solution alternating daily with 15 gr *per os* has been found of value for the relief of pain in cancer. A solution of 3 to 5 gr. per oz. may be used for irrigation of a liver abscess cavity after exploratory aspiration, and may render operation unnecessary.

**CHRONIC CONSTIPATION.** Rectal use best—5-gr suppositories —*Brit med J Epit.*, 1/1930, 8

**PNEUMONIA.** Treatment by quinine dihydrochloride intravenously (7 grains in 10 ml) —R. Kharegab, *Lancet*, 11/1925, 626

**PURPERAL SEPSIS.** One or two injections of 10 gr produced good results —P. Liston, *Brit med J*, 11/1927, 959.

On the first 3 or 4 days one injection intravenously and subsequently intramuscularly, using a solution of 5 gr in 10 ml —S. G. Luker, *Brit med J*, 1/1930, 261, see also A. C. Hill, *ibid*, 270

### **Intravenous Injection of Quinine Acid Hydrochloride in Malaria.**

**Dose.**—An average dose may be considered as from 4 to 15 grains (0.25 to 1 g.), though some hold that neither the intramuscular nor the intravenous dose should exceed 5 grains.

**Dilution.** Some use an exceedingly dilute solution (*e.g.*, as low as 1 in 300). Others advise even a 10% solution. Newton Pitt advised 1 in 40.

**Rate of injection.** This, as with all intravenous injections, should be slow

**DANGER OF RAPID INTRAVENOUS INJECTION of quinine solution in malaria**  
There may be dangerous fall of blood pressure with concentrated solution. The whole problem turns on the amount of quinine passing through the heart every second. The amount of quinine injected into a vein at the bend of the elbow should not be more than  $\frac{1}{10}$  gr per second or  $\frac{1}{2}$  gr a minute. 10 gr will require 20 minutes. The solution should not exceed strength of 1 in 300—to be given at the rate of 10 ml per minute for patients over 15 years of age. Half rate for children under 15. Tables showing effect on systolic, diastolic and pulse pressures after intravenous injections of dilute solutions of quinine dihydrochloride—U N Brahmachari, *Lancet*, 11/1922, 175, *J trop Med (Hyg)*, 1922, 209.

Malaria is not more readily cured by intravenous medication. 90% of the quinine injected intravenously disappears from the blood within one minute and is stored in the tissues, but intravenous medication will always have a more or less restricted field of usefulness—*Brit med J. Epit*, 11/1922, 33.

Quinine intravenously  $\frac{1}{2}$  to 1 g, in 40 to 50 ml of saline, 2 to 10 times daily, gave good results in 164 cases of malaria, no general or local reactions or complications—*Per Prescriber*, 1926, 28.

Quinine dihydrochloride efficacious intravenously in acute and chronic malaria, and in cases in which malaria complicates other diseases also used in pneumonia and septicæmia with success—B Rattan, *Brit med J*, 11/1927, 39.

**CEREBRAL MALARIA** On the earliest appearance of cerebral symptoms 10 grains of the acid hydrochloride intravenously in 20 ml of diluent saved many lives—A G Phear, *Lancet*, 1/1920, 195.

Intramuscular injections condemned in ordinary cases of malaria, but intravenous injections (quinine dihydrochloride 0.6 g in 5 ml physiological saline) recommended in serious cases of malignant tertian associated with persistent vomiting or threatened coma—S. P James, *Brit med J*, 11/1933, 929.

### **Intramuscular Injection of Quinine in Malaria.**

Hundreds of intramuscular injections of quinine given over a period of 19 years without a single distressing result. Injections always given in the gluteal region, choosing the highest point where the muscle is deep enough to sink the needle in—not the ordinary short hypodermic needle, but one long enough to make sure of giving the injection well into the muscle. Injections should never be given into the arm—R A Murphy, *Indian med Gaz*, 1925, 48.

Muscular necrosis an invariable occurrence with intramuscular administration of quinine in malaria. Damage is intensified, in case of alkaloid, by use of solvents such as ether, alcohol, olive oil or creosote, and natural fat. Necrosis evident one hour after injection in man, and within 10 minutes in animals—*J trop Med (Hyg)*, 1923, 12.

Intramuscular use of quinine salts was condemned by the Medical Service of the E A E F—A R Balmain, *Brit med J*, 1/1920, 381.

Necrosis of muscle caused by quinine injections into the buttocks—it was not possible to determine form of quinine—P Figdor and D D Pinnock, *Brit med J*, 11/1922, 14.

Intramuscular injection of salts of quinine should be considered as malpraxis, as tissue is unable to live in presence of these bases at a high concentration, 1:12, 1:2000, and there is a danger of tetanus with imperfect sterilisation. Oral method the only method of administering cinchona alkaloids, though rarely in grave cases, e.g., cerebral malaria, quinine base should be injected intravenously—H W Acton and R N Chopra, *Indian J med Res*, Oct, 1924, 251, see also J. Macqueen, *Lancet*, 1/1927, 1289.

Intramuscular injections given in large numbers without tetanus being caused (as result of muscle fibre necrosis). Pain does not occur unless some solution gets into the subcutaneous tissues. However, intravenous injections are more rapid and painless. 0.6 g in 10 ml water—M S Nawaz Ahmadi, *Brit med J*, 11/1930, 621.

**Lotio Quininae Hydrochloridi (R L O H)** Quinine dihydrochloride 4 gr, sterilised water to 1 oz. For corneal ulcers.

[D P I 81] **"Old English" Fever Powder.** Quinine dihydrochloride 3 gr, arsenious acid  $\frac{1}{4}$  gr, compound soap pill 1 gr, calomel  $\frac{1}{16}$  gr. 3 times daily in a cachet. Malaria well treated. The following [D P I 81] daily dose made up in the form of a pill recommended as prophylactic—Quinine dihydrochloride  $\frac{1}{4}$  gr, arsenious acid  $\frac{1}{16}$  gr, compound soap pill  $\frac{1}{16}$  gr, calomel  $\frac{1}{16}$  gr—*J. trop. Med. (Hyg.)*, 1922, 265.

**Quininæ Dihydriodidum (B.P.C.).**

$C_{20}H_{24}O_2N_2 \cdot 2HI \cdot 5H_2O = 670 \cdot 2$  *Syn.* QUININÆ HYDRIODIDUM ACIDUM.

*Dose.*—1 to 5 grains (0.06 to 0.3 g.).

Pale yellow crystals or scales, soluble 1 in 20 of water.

**Quininæ Disalicylosalicylas (B.P.C.) *Syn. and Prop. Names.***

QUININÆ BISALICYLOSALICYLAS, QUINISAL (*Boehringer, Mannheim*), QUINISAN (*Howards, Ilford*).

$C_{20}H_{24}O_2N_2 \cdot 2C_6H_4(COOH) \cdot O \cdot CO \cdot C_6H_4(OH) = 840 \cdot 4$ .

*Dose.*—1 to 5 grains (0.06 to 0.3 g.).

White microcrystalline powder with slightly bitter taste. Contains about 39% of anhydrous quinine. For influenza, coryza, tonsillitis, neuralgia, etc.

**Quininæ et Æthylis Carbonas (B.P., U.S.P. XI, P. Jap. IV, P. Helv. V, P. Ned. V, F.E. VIII, P. Belg. IV, P. Ital. V)**  
 $C_{20}H_{23}O_2N_2 \cdot CO_2 \cdot C_2H_5 = 396 \cdot 2$ . *Prop. Name.* EUQUININE (*Bayer Products, London*).

*Dose.*—1½ to 15 grains (0.1 to 1 g.) in cachet. F.E. VIII gives max. *per diem* 1 drachm approx.

White needle crystals, m.p. 90° to 92° (B.P. Add. not below 90°), with little taste. Soluble sparingly in water, more so by addition of dilute acid; soluble 1 in 2 of alcohol 90%. Intended to replace quinine owing to its freedom from bitterness.

Whooping cough has been treated with it.

**Aristoquinine.**  $CO(C_{18}H_{17}O_2N_1)_2 = 674 \cdot 4$ . *Syn. and Prop. Name.* CHININUM CARBONICUM (P. Ital. V, P. Ned. V), ARISTOCHIN (*Bayer Products, London*).  
*Dose.*—1 to 10 grains (0.06 to 0.6 g.) according to age.

A white tasteless powder. Obtained by heating quinine with phenyl carbonate, and containing 96.1% of quinine. Insoluble in water. Used in malaria, typhoid, influenza and pertussis as a tasteless substitute for quinine. Incompatible with acids and alkalis.

**Quininæ et Ureæ Hydrochloridum (B.P.C., U.S.P. XI).**  
 $C_{20}H_{24}O_2N_2 \cdot HCl \cdot CO(NH_2)_2 \cdot HCl \cdot 5H_2O = 547 \cdot 3$  *Syn.* QUININÆ HYDROCHLORO-CARBAMIDUM, UREA-QUININE

*Dose.*—½ to 15 grains (0.03 to 1 g.), by injection. U.S.P. XI average hypodermic dose (once daily) 15 grains.

In small prisms, soluble 1 in about 1 of water. Contains about 59% of anhydrous quinine.

**Uses.** Intramuscularly, in malaria and in cholera. Mainly used as a local anæsthetic in doses of 3 to 5 ml. of 0.5 to 1% solution, especially for rectal operations where post-operative pain is severe, since its anæsthetic effect may last for several hours or even days. For internal hæmorrhoids the 5% is used, using a few minims for each pile, or the whole area may be treated by submucous injection. The injection of 4 m. of the 5% solution, repeated if necessary at 2 to 3-day intervals, has been used in anal fissure. For local application strong solutions (10 to 20%) must be used to ensure passage through the mucous membrane, and have been found of value in tonsillitis and painful throat affections.

Apply by spray, sponge, brush, etc. A teaspoonful or so of solution may be taken in the mouth and used to bathe the tonsils by swaying the head from side to side. Deep intramuscular injection of 5 ml of 1% solution is useful in lumbago, sciatica and neuritis.

**EXOPHTHALMIC GOITRE** and thyroid enlargement treated by injections of 4 to 8 ml. of a 4% solution of quinine and urea hydrochloride into the thyroid. After a few treatments the goitre becomes smaller and when it is one-third of original size the treatment can be stopped, as the shrinking will continue until no tumour is perceptible. The drug is believed to act through its necrotic action on the parenchyma of the gland.—H. G. Loughran, per *Prescriber*, 1927, 173.

**HÆMORRHOIDS** The injection is to be given between the vein and the mucous membrane of the rectum, and not in the vein itself. It is seldom necessary to give more than 3 ml at one sitting. Injections given at weekly intervals, 6 to 8 being the average number required.—C. Howard, *Lancet*, 1/1929, 20.

Sloughing after 5% injection in hæmorrhoids. Never inject an external pile or a prolapsed pile without first reducing it and never inject a pile that is already sclerosed.—*Lancet*, 1/1930, 1027.

**HYDROCELE** The injection treatment of hydrocele is favourably reported upon on all sides, the best sclerosing agent being quinine and urea hydrochloride, 3 to 5 ml. The hydrocele is tapped, after washing out the sac with more saline the solution is introduced into the hydrocele sac. The scrotum is then massaged. Although the fluid in the sac reaccumulates, within 3 or 4 weeks the exudate is generally absorbed.—H. Bailey, *Med Annu*, 1935, 429.

**PRURITUS ANI, VULVÆ, AND SCROTI**, well treated as follows: render part clean, apply mercurochrome solution as antiseptic, inject small area with not more than 10 ml. of 1% procaine hydrochloride, inject  $\frac{1}{4}$  gr. morphine hypodermically, infiltrate remainder of diseased skin with quinine and urea hydrochloride solution 0.25 to 0.5% (as much as 200 to 300 ml. may be used). Itching arrested, excoriations healed and skin becomes normal in few days.—*J. Amer. med. Ass.*, 11/1924, 766.

**SCIATICA** Injection into sciatic nerve, where it crosses neck of femur, of 1% solution of quinine and urea hydrochloride, specific for sciatica.—*Brit. med. J. Epit.*, 11/1926, 96.

**WOUNDS.** For wounds which are to heal by granulation, quinine urea hydrochloride 1 in 600 should be liberally injected as a prophylactic against pain.—R. E. Farr, *Lancet*, 11/1929, 1199.

**Quininæ Formas Acidus** ("Neutral" in France).

$C_{20}H_{24}O_2N_2 \cdot (H \cdot COOH)_2 = 416.2$ .

*Dose.*—1 to 5 grains (0.06 to 0.3 g.).

Long white needles containing 77.9% of quinine; m.p. 95°.

**Quininæ Formas** ("Basic" in France).

$C_{20}H_{24}O_2N_2 \cdot H \cdot COOH \cdot H_2O = 388.2$ . *Syn. and Prop. Name.* QUINOFORM, CHINOFORM (*Chinosolfabrik, Hamburg*; *C. Zimmermann, London*).

*Dose.*—1 to 5 grains (0.06 to 0.3 g.). Subcutaneously, 1 to 3 grains. (Stated not to be painful.)

Prepared by using a very small quantity of water, in which the quinine is placed and the acid added. White crystals, m.p. about 126°, containing 87.5% of quinine. A general tonic. Suitable for hypodermic use. *Guttæ* 1 in 50 have been employed satisfactorily in asthenopia.

**Solubility** varies according to conditions of manufacture. Some commercial samples are only soluble 1 in 600 of water and 1 in 110 of alcohol. A 1 in 20 solution can be made extemporaneously by dissolving 1 g. of the base in 19 ml. of water containing 0.125 g. of formic acid.



**Quininæ Hydrilodidum (B.P.C.).**  $C_{20}H_{24}O_5N_2 \cdot HI = 452.1$   
*Syn.* QUININE IODIDE.

*Dose.*—1 to 5 grains (0.06 to 0.3 g.).

Pale yellow crystals slightly soluble in cold water, readily in hot water and in alcohol.

**Quininæ et Urethani Hydrochloridum.**

*Dose* — $\frac{1}{2}$  to 3 grains (0.03 to 0.2 g.).

Employed hypodermically, as it is non-irritating.

Obtained by heating quinine hydrochloride 3 with urethane 15 and water 3 parts. For quinine and urethane injection treatment of varicose veins, *see below*.

**Injectio Quininæ et Urethani (B.P.C.).**

*Dose.*—75 minims (5 ml.), by intravenous injection.

Quinine hydrochloride about 13.5% *w/v* and urethane about 6.5% *w/v* in water.

A green colour may develop in quinine and urethane injections due to the presence of traces of copper in the latter—O. Tonn, *Pharm Zentralh*, 1933, 74, 53.

ANGIOMA OF THE LOWER LIP treated by 14 injections over 6 months, commencing with 0.5 and increasing to 1 ml. Injections through sound skin near margin of tumour. Treatment painless—Graham, *J. R. A. M. C.*, April, 1930.

HÆMORRHOIDS treated with quinine hydrochloride 0.8 g., urethane 0.4 g. in normal saline 2 ml.—Bellot, *Lancet*, 1/1929, 1072.

Good results by injection of 3 to 5 ml. of 5% solution perivenously (into the submucous tissue round the piles), repeating the injection at weekly intervals on opposite sides—A. H. Douthwaite, *The Injection Treatment of Varicose Veins* (H. K. Lewis), 5th Edn., 1929.

HYDROCELE OF THE TUNICA VAGINALIS treated by injection of quinine-urethane solution 2 ml. without pain or discomfort—F. C. Pybus, *Brit med J*, 1/1930, 239.

NÆVI cured by injection of a minim of quinine and urethane solution into 4 or 5 different places in the nævus, repeated two or three times at fortnightly intervals—G. B. Dowling, *Lancet*, 11/1929, 1251, *Med Annu*, 1931, 324.

Cavernous nævi involving the left breast and the buttock, in a girl aged 9 months, successfully treated by this method. Excision should be relegated to the past.—A. P. Bertwistle, *Lancet*, 1/1934, 22.

VARICOCELE successfully treated by quinine-urethane injection (Douthwaite's formula)—one injection of 1 ml.—H. M. Hanschell, *Brit med J*, 11/1928, 915.

### **Quinine and Urethane Injection Treatment of Varicose Veins.**

The quinine-urethane method was originally popularised by Genevriér in France. The injection contains quinine hydrochloride 4 g., urethane 2 g. in distilled water 30 ml. (Injectio Quininæ et Urethani B.P.C.). The solution can be boiled and is strongly antiseptic. It crystallises out when cool but redissolves on immersing in hot water for a few seconds.

*Contraindications.* Deep thrombosis, acute phlebitis, intra-abdominal tumours, cardiovascular disease, skin diseases, pregnancy. The injection should not be given during menstruation.—R. T. Payne, *Lancet*, 11/1929, 313.

*Initial Injection*  $\frac{1}{2}$  ml., and subsequently 2 to 3 ml. Injections may be given with the patient sitting or lying down—in the latter case, a pneumatic tourniquet is applied to the middle of the thigh

before the patient lies down. Clean the skin with ether and introduce needle of syringe not quite filled with solution into the lowest segment of the vein, the skin overlying the vein being drawn aside before introducing the needle. Withdraw the piston slightly and allow blood to flow into the barrel before any fluid is introduced. Inject  $\frac{1}{4}$  to  $\frac{1}{2}$  ml. according to size of vein and hold needle in position for 30 seconds before withdrawal. Press a pledget of wool on puncture and repeat the process 4 inches up the limb. When the total number of injections has been given, clean with ether and seal punctures with collodion dressings. Sitzings are given at weekly intervals, 6 sittings usually sufficing. Injections may be successfully given, without fear, in the region of the saphenous opening.

Injections of 2 ml. can generally be relied on to thrombose 5 to 6 inches of a vein. Injections are needed at approximately 4 to 5 inches along the course of a vein. In this way the whole saphenous tract may be treated to within about 4 inches of the saphenous opening.

From an experience of 3000 cases over 11 years, quinine-urethane and sodium salicylate are the drugs of choice for injection treatment, and sodium morrhuate does not possess all the virtues once claimed for it—S. McAusland, *Brit. med. J.*, 11/1933, 529.

Quinine-urethane solutions appear to be the most certain in their thrombosing action, with the empty-vein technique and small doses they are extremely efficient. Quinine-urethane solutions have the additional advantage of being painless during injection. Salicylate solutions, on the other hand, are invariably extremely painful during the actual injections, and they are much less certain in their action, owing to the rapid development of tolerance on the part of the veins towards them. Sodium morrhuate suffers from two disadvantages: first, it is necessary to add 0.5% phenol to ensure sterility of the solution, and, secondly, it is certain that in some instances thrombosis occurs immediately after injection—R. T. Payne, *Brit. med. J.*, 1/1936, 878.

### *After-effects.*

Patients should be told that *small and thin-walled veins will swell up* rapidly to four times their original size. The swelling passes off in a few hours and is of no importance. *Sensations of fullness, aching or tenderness* sometimes occur lasting three or four days; *a feeling of contraction* of the leg, one month after obliteration of the internal saphenous vein, passes off in a few weeks. *Edema of foot and leg* occurs in about 2% of cases from 5 to 7 days after injection, persisting for some two weeks. *Itching of the overlying skin* (following treatment by any sclerosing solution) is relieved by application of ichthammol and Lassar's paste.—A. H. Douthwaite, *The Injection Treatment of Varicose Veins* (H. K. Lewis), 5th Edition, 1929.

Over 6000 injections, given without the production of embolic mishap, are sufficient testimony to the safety of one of the greatest additions to modern therapeutics—A. H. Douthwaite, *ibid.*

May cause cramp 5 or 6 hours after. Clot remains red and painful for 6 weeks. With thin-walled veins action severe.—D. Levi, *Lancet*, 11/1930, 16.

The danger of the embolic action of quinine in pregnancy has been greatly exaggerated. Twenty-five cases of varicose veins in pregnancy (ranging from fourth week to term) treated by weekly injections of 1 ml. of quinine-urethane solution containing 0.133 g. quinine HCl, increased up to 0.798 g. at a single

injection. One case of cinchonism occurred but was not associated with uterine symptoms.—R. Greene, *Brit. med. J. Epit.*, 1/1933, 15.

**LATE RESULTS OF INJECTION TREATMENT** Of 50 cases re-examined at the Middlesex Hospital 2 or more years after injection (quinine-urethane) in only 10% had a "cure" resulted in the sense that the patient had been made free and remained free of symptoms and signs up to the time of re-examination. It is evident that recanalisation of obliterated veins is a frequent event and a common cause of recurrence, and injection treatment should be regarded as a useful means of palliation rather than as a cure; original estimates were too enthusiastic. The present tendency is to combine surgical treatment with injections as a means of shortening the time of treatment and in hope that end-results will be better. The present practice at the Middlesex Hospital is to remove a segment of the main superficial vein, where it can be shown that pressure on it in the standing position controls the superior reflux and to follow up with injections to the peripheral veins.—D. Patey and R. C. Tatham, *Brit. med. J.*, 11/1933, 862

**Perivenous Administration.** The needle is first introduced into the lumen of the vein and then withdrawn until its point is felt to slip out of its wall into adjacent tissues, when 2 minims of solution are injected. There is immediate but transient pain and subsequent swelling, redness, tenderness and local oedema, usually passing off within a week. This method is rarely necessary, but of value in dealing with large isolated dilatations. It should never be made with solutions other than those of quinine.—A. H. Douthwaite, *The Injection Treatment of Varicose Veins* (H. K. Lewis), 5th Edn., 1929

**Giemsa's Injection** contains quinine hydrochloride 10 g., urethane 5 g., water 18 ml. The volume of the product is 30 ml., so that 1.5 ml. of solution contains 0.5 g.

**Solutio Quininae et Urethani** (for varicose veins) (*St. T. H.*)

*Dose*—5 ml. intravenously.

Quinine hydrochloride 5% and urethane 2½% in distilled water

**Sterules Quinine and Urethane** (*Martindale, London*) Ampoules containing 2 ml. of quinine and urethane solution for the injection treatment of varicose veins

**Varixol** (*Evans, Sons, Lescher & Webb, Liverpool*) Quinine and urethane solution for the injection treatment of varicose veins

**Quininae Hydrobromidum** (*B.P.C.*) (*P. Belg. IV, Fr. Cx and P. Ital. V* term this "basic" quinine hydrobromide.)

$C_{20}H_{24}O_2N_2 \cdot HBr \cdot 2H_2O = 441.2$ . *Syn.* QUININE BROMIDE.

*Dose*.—1 to 10 grains (0.06 to 0.6 g.) or more.

White acicular crystals, soluble 1 in 55 of water, 1 in 0.7 of alcohol 90%.

Contains not less than 73% of anhydrous quinine. Quinine is given with an excess of hydrobromic acid to lessen the cinchonism sometimes caused by large doses. Is valuable in acute rheumatism. In malaria for oral administration, hypodermically or intravenously, also in exophthalmic goitre. Tropical abscess has been treated by aspiration and injecting into the cavity a 1% solution.

**EXOPHTHALMIC GOITRE** Quinine hydrobromide in 2½-gr doses thrice daily one of the best treatments.—J. B. Alexander, *Clin. J.*, 1923, 394

**Quininae Hydrochloridum.** (*B.P., P. Helv. V, P. Jap., P. Dan., P. Hung., P. Ital. V, P. Ned. V., P.G. VI.*) *F.E. VIII, P. Belg. IV and Fr. Cx.* term this "basic" quinine hydrochloride  $C_{20}H_{24}O_2N_2 \cdot HCl \cdot 2H_2O = 396.7$ . *Syn.* QUININE HYDROCHLORATE

*Dose*.—1 to 10 grains (0.06 to 0.6 g.). *F.E.* has max. daily dose 2 g.

This salt contains 81·7% base against 73·5% in the sulphate  
Efflorescent in warm air

**Soluble** 1 in 32 of water, 1 in 2 of 90% alcohol. Quinine hydrochloride 2 with phenazone 1 will dissolve in 4 of water.

**Incompatible.** Similar to quinine sulphate

**Uses.** It is sometimes better tolerated than the sulphate. Subcutaneous or intravenous injections useful where not tolerated by the mouth

For the paroxysmal headache or neuralgia so common after malaria the following mixture is recommended:—Quinine hydrochloride 3 gr, tincture of cinicifuga 5 m, caffeine citrate 2 gr, spirit of chloroform 10 m., compound infusion of orange to 1 oz, twice daily

In acute tonsillitis, quinine hydrochloride internally and as mouth-wash is useful; also with dilute nitric acid in cachectic cases of vesicular stomatitis. In conjunction with urethane, quinine hydrochloride is extensively used in the injection treatment of varicose veins, *see* p 820.

**LOCAL ANÆSTHESIA IN TONSILLECTOMY** Quinine hydrochloride  $\frac{1}{2}$  gr in 2 dr of water superior to 0·2% cocaine (5 ml) A small amount of 20% cocaine first applied —E J. Brown, *J Amer med Ass*, 11/1923, 321

Quinine and all its derivatives are general protoplasmic poisons, and in proportion as they exert this action, they act as local anæsthetics —W E Dixon and Premankur De, *J Pharmacol*, Oct, 1927, 407

**Collyrium Quininae Hydrochloridi (B P C.).** 0·5% w/v.

**Mistura Quininae cum Ferro.**

**Dose** — $\frac{1}{2}$  ounce thrice daily in water 30 minutes after food

Quinine hydrochloride 30 gr, tincture of ferric chloride  $\frac{1}{2}$  oz, glycerin 1 oz, water to 8 oz.

Bad cases of secondary syphilis do well on this

[P1] **Mistura Quininae et Magnesia Sulphatis (L H)** Quinine hydrochloride 1 gr, magnesium sulphate 30 gr, dilute hydrochloric acid 1 m, solution of arsenic 3 m, solution of strychnine hydrochloride 3 m, water to 1 oz For use during treatment of stomatitis and gingivitis

**Nebula Quininae.** Quinine hydrochloride 10 gr glycerin and rose water to 1 oz

**Pessus Quininae Hydrochloridi** contains 3 gr (0·2 g) in 30 gr of oil of theobroma A valuable remedy for leucorrhœa Also used as a contraceptive

Contraceptive action of pessaries with cocoa butter basis probably largely due to mechanical action, *i e*, the covering of the cervix with a thin film impeding the ingress of the spermatozoa —*Lancet*, 11/1931, 258

At the B M A Cent Meeting, 1932 (Sect of Dermat and Vener Dis) several speakers quoted cases of dermatitis, due to quinine idiosyncrasy, following the use of quinine pessaries —*Lancet*, 11/1932, 399

Now that substances are available which are not only more spermicidal but also free from any harmful and remote effects on the users, it would seem that the time has come to abandon the use of quinine for contraceptive purposes —*Lancet*, 11/1935, 1133.

**Rendell's Quinine Pessaries (W. J Rendell, London)** Pessaries weigh 36·6 gr. and contain 3·5% of quinine, equivalent to 2·16 gr. of quinine acid sulphate. —Vogel, *Chemistry and Physics of Contraception*

Where cocoa butter hinders the action of Chinosol and quinine on sperms a new fat called **Cococala**, which is nearly odourless, has not this defect —J. R Baker, *Lancet*, 11/1931, 325. **Vimule Pessaries (A. Lambert & Sons, London)** are stated to be made with this.

*For further references to contraceptives, see Potassii Hydroxy-quinolini Sulphas, p 796*

[D P1 81] **Pulvis Quininae, Arseni, Hydrargyri et Ipecacuanhae Compositus.**

Quinine hydrochloride 5 to 7 gr, arsenious acid  $\frac{1}{8}$  to  $\frac{1}{2}$  gr, Dover's powder 3 to 4 gr, calomel  $\frac{1}{10}$  to  $\frac{1}{4}$  gr. In a cachet, one to be taken at 11 a.m. and another at bedtime

In chronic malaria with enlarged spleen

**Soluté de Quinine pour injection hypodermique (Fr. Cx)**

Quinine hydrochloride 3 g, phenazone 2 g, water to 10 ml. Special instructions as to sterilisation are provided

**Tinctura Quininae (B.P.C.).** *Dose.*— $\frac{1}{2}$  to 1 drachm (2 to 4 ml.).

Quinine hydrochloride 1, tincture of orange 50. A very agreeable form of taking small doses of quinine

**Vinum Quininae (B.P.C.).** *Dose*— $\frac{1}{2}$  to 1 ounce (16 to 30 ml.).

Contains 1 gr of quinine hydrochloride dissolved in 1 oz of orange wine.

*The Customs and Excise Commissioners allow the sale of quinine wine without licence if—(a) It is prepared in accordance with the B.P.C.; (b) Sales are made only by duly qualified chemists and druggists, and (c) It is labelled to show that it is to be used as a medicine. The word "Dose" should appear on the label in bold type. This should not exceed the B.P.C. dose, but the Board do not object to the use instead of the words "one or two tablespoonfuls," or "half a wineglassful"*

**Solvochin (Homburg Pharma Ltd, London)** Water-soluble quinine ("quinine-hydrate-phenazone-basic quinine-hydrochloride") *Dose*—In pneumonia, 2 ml daily on 3 successive days, intramuscularly, in malaria and obstetrics (to promote uterine contraction), 1 or 2 intramuscular injections of 2 ml daily

**Sterules Quinine-Mannitol (Martindale, London)** Ampoules containing 2 ml of a solution of quinine alkaloid 12 g, boric acid 8.4 g, mannitol 7.5 g, water to 100 ml. A solution of basic quinine for injection in place of acid solutions *Dose*—1 to 2 ml

**Quininae Hypophosphis (B.P.C.)**

$C_{20}H_{24}O_2N_2, H_3PO_2, 2H_2O = 426.3$

A white crystalline or amorphous powder, soluble 1 in 24 of water and 1 in 40 of alcohol 90%. Contains about 75% of anhydrous quinine

**Quininae Lactas (B.P.C.)**

$C_{20}H_{24}O_2N_2, CH_3 \cdot CHOH \cdot COOH = 414.3$  *Dose*—1 to 5 grains (0.06 to 0.3 g)

A crystalline or granular white powder, soluble 1 in 6 of water. Said to be well tolerated, is suitable for hypodermic injection. For gonorrhœa, 1% solution forms an excellent injection

Contains not less than 72% of anhydrous quinine

**VARICOSE VEINS**—Preferable to the hydrochloride which is apt to cause severe reactions. Employed as a 10 or 15% solution, also as a saturated solution (16.6%) on 170 patients, with good results. It is self-sterilising in solutions above 1% and solutions keep well. The dose for each injection varies from 0.25 to as much as 3 ml in large veins. —J. W. Riddoch, *Lancet*, 11/1934, 1101

**Quininae Nucleinas.** *Dose.*—1 to 5 grains (0.06 to 0.3 g.)

Yellowish powder containing 60% quinine and 40% nucleinic

acid Insoluble in water In syphilis has been employed as 5% suspension in olive oil Intramuscular injections of 10 ml. were used, assisted by intravenous injections of the hydrochloride

**Quininæ Phosphas** (*B P C*)

$(C_{20}H_{24}O_2N_2)_3 \cdot 2H_3PO_4 \cdot 6H_2O = 1277.0$  Dose.—1 to 5 grains (0.06 to 0.3 g.)

In acicular crystals like the sulphate, but harder and denser Contains about 75% of anhydrous quinine Soluble 1 in 850 of water and 1 in 110 of alcohol 90%

**Quininæ Salicylas** (*B P C.*, *F.E. VIII.*, *P. Ital. V*)

$C_{20}H_{24}O_2N_2 \cdot C_6H_4(OH)COOH \cdot H_2O = 480.3$

Dose —1 to 5 grains (0.06 to 0.3 g.).

White crystals, sparingly soluble in water, and about 1 in 24 of alcohol 90% Incompatible with mineral acids—salicylic acid may crystallise out Contains 68.8% of quinine Should be given in cachets, or pills made with syrup of glucose, or as quinine salicylate mixture Given to abort the common cold, in influenza and in neuralgia, rheumatism and sciatica

**Mistura Quininæ Salicylatis** (*B.P.C.*)

Dose — $\frac{1}{2}$  to 1 ounce (15 to 30 ml)

Contains ammoniated solution of quinine 30 m., sodium salicylate 10 gr, and potassium citrate 10 gr in glycerin and compound infusion of gentian to 1 oz.

**Quininæ Sulphas** (*B P*). (Termed "BASIC" QUININE SULPHATE in *Fr Cx.*, *P. Ital. V.* and *F.E. VIII.*)

$(C_{20}H_{24}O_2N_2)_2 \cdot H_2SO_4 \cdot 7\frac{1}{2}H_2O = 881.6$ . *Fr Cx.*, *P. Jap.*, *F.E. VIII.*, *P. Ital. V.*, *P. Ned. V.* and *P.G. VI.*,  $8H_2O$ , *P. Belg.*,  $7H_2O$ , *U.S.P. XI* and *P. Helv. V.*,  $2H_2O$ ; *P. Dan.*, 7 to 8  $H_2O$

Dose —1 to 10 grains (0.06 to 0.6 g.). *U.S.P. XI* average dose 15 grains *F.E. VIII* gives max daily dose 2 g

White silky crystals containing about 75% of anhydrous quinine

**Soluble** 1 in 800 of cold water, 1 in about 65 of alcohol 90%, 1 in 40 of glycerin It is rendered more soluble by the addition of phenazone

Water content varies among the National Pharmacopœias, *v. supra* The dihydrate containing 4.5 to 4.7% water should be international—*R. Eder, Pharm J.*, ii/1930, 242

It is prescribed in pill, cachet, tablet or mixture—if in mixture 1 m. of dilute sulphuric acid per gr of sulphate will render more soluble (with fluorescence). For pills 1 drop of strong sulphuric acid as excipient for 5 gr

**Incompatible** with alkalis and alkaline carbonates, also incompatible with Liquor Ammonii Acetatis (unless distinctly acid in reaction), iodides and astringent infusions containing tannin The addition of a small proportion of sodium hypophosphite may overcome the incompatibility with potassium iodide (due to the formation of quinine iodosulphate or herapathite) To prevent coagulation of the precipitate when prescribed with alkalis,

mucilage of acacia should be ordered. With phenol in a pill may liquefy.

**Prescribing Note.**—To overcome the taste to some extent it may be given as *Mistura Quininae Effervescens*. Liquid extract of eriodictyon in  $\frac{1}{2}$  dr. doses also removes the bitterness.

**Uses.** For all forms of fevers and as prophylactic; wards off remittent fever. For neuralgia and nervous headache; it combats whooping-cough, influenza (usually given as the ammoniated solution) and hay-fever. It increases uterine action, and is the most used tonic drug; antiseptic in typhoid, phthisis and pneumonia. Pills of quinine, atropine, and arsenic (*q v.*) will frequently stop the development of a "cold." If quinine deafness occurs, or for large doses, hydrobromic acid should be used. In labyrinthine disorders, it is very uncertain—often intensifying the symptoms

**Capsulae Quininae Ammoniatæ (B.P.C.).** Dose —1 capsule

Contain quinine sulphate and ammonium bicarbonate approximately equivalent to 1 dr. of ammoniated solution of quinine

**Capsulae Quininae Ammoniatæ et Cinnamomi (B.P.C.).**

Dose.—1 capsule.

Similar to the preceding but containing also  $\frac{1}{4}$  m. of oil of cinnamon.

**Capsulae Quininae et Cinnamomi (B.P.C.).** Dose —1 capsule

Quinine sulphate 1 gr., oil of cinnamon 1 m.

**Collunarium Quininae.** Quinine sulphate 1, water 1000

Used in hay-fever. If a stronger solution be required, use the acid sulphate or hydrochloride of quinine, avoid excess of acid.

**Elixir Quininae Ammoniatum et Cinnamomi (B.P.C.).**

Dose.— $\frac{1}{2}$  to 1 drachm (2 to 4 ml.).

A flavoured preparation of approximately the same strength as ammoniated solution of quinine and containing also oil of cinnamon.

**Liquor Quininae Ammoniatæ (B.P.).** *Syn.* TINCTURA

QUININÆ AMMONIATÆ. Dose — $\frac{1}{2}$  to 1 drachm (2 to 4 ml.).

Quinine sulphate 2% and dilute solution of ammonia 10%, in alcohol (60%). The quinine precipitates on adding to water, mucilage of tragacanth will suspend the precipitate. With syrup of orange it is palatable, and bears dilution better; it remains bright if mixed with aerated water. Should be kept in the dark, or it will become discoloured.

**Ammoniated Quinine Tablets** are prepared, each equivalent to 1 drachm of the preceding solution

Ammoniated quinine tablets Analysts' findings on trade varieties Ammonia likely to be lost —*Pharm. J.*, 1/1931, 499.

**Mistura Chlorigum Quinina (Burney Yeo)**

To potassium chlorate, in powder, 30 gr., in a 12-ounce bottle, add hydrochloric acid 60 m., cork and shake well to liberate chlorine, absorb this by gradually adding, and shaking after each addition, distilled water *q s* to 11 oz., add quinine sulphate 24 gr. (or 36 gr. if ordered), syrup of orange 1 oz. Dose — 1 ounce (30 ml.) every 2, 3, or 4 hours for typhoid; it quickly cleanses the tongue

**Mist. Ferri et Quin. (N.I.F.).** Quinine sulphate 1 gr., solution of ferric chloride 10 m., dilute hydrochloric acid 1 m., chloroform water to  $\frac{1}{2}$  oz.

**Mistura Quininae Ammoniata (St. M. H.).**

*Dose.*— $\frac{1}{2}$  to 1 ounce (15 to 30 ml).

Ammoniated solution of quinine 1 dr., dilute solution of ammonium acetate 2 dr., sodium nitrite 1 gr., mucilage of tragacanth 1 dr., chloroform water to 1 oz

**[P1] Mistura Quininae Composita (L.H.) Syn BROADBENT'S MIXTURE.**

Ammoniated solution of quinine 1 dr., strong solution of ammonium acetate 15 m, camphorated tincture of opium  $\frac{1}{2}$  dr, ammonium carbonate 2 gr, tragacanth  $\frac{1}{2}$  gr, peppermint water to  $\frac{1}{2}$  oz

**Mistura Quininae Effervescens.**

Quinine has a reputation in colds, but it is best given in effervescence. The following prescription is useful—

*Mixture A*—Quinine sulphate  $2\frac{1}{2}$  gr., citric acid 10 gr, water to  $\frac{1}{2}$  oz

*Mixture B*—Potassium bicarbonate 10 gr, ammonium carbonate  $2\frac{1}{2}$  gr, syrup of orange 1 dr, water to 1 oz

One tablespoonful of mixture (A) with two of mixture (B) in effervescence thrice daily—Leonard Williams, per *Chem & Drugg*, June, 1921

**[P1] Mist. Quin. et Gelsem. (NIF)** Quinine sulphate  $1\frac{1}{2}$  gr, potassium bromide  $7\frac{1}{2}$  gr, dilute hydrobromic acid  $7\frac{1}{2}$  m, tincture of gelsemium  $7\frac{1}{2}$  m, water to  $\frac{1}{2}$  oz

**Mist. Quin. Sulph. (NIF).** Quinine sulphate  $1\frac{1}{2}$  gr, dilute hydrobromic acid 10 m, concentrated infusion of orange  $7\frac{1}{2}$  m, water to  $\frac{1}{2}$  oz

**[D P1 S1] Pilula Quininae Hydrargyri et Opil.**

Quinine sulphate  $1\frac{1}{2}$  gr, grey powder 1 gr, opium  $\frac{1}{2}$  gr, quassia extract  $q s$ , thrice daily after food.

In syphilis quinine is useful before or after a course of mercury

Acts beneficially in any septicæmic state with fever, whether due to gonorrhœa, syphilis, or enteric Quinine, opium and mercury are sheet anchors in early syphilis

**Pilula Quininae Sulphatis (B P C)** *Dose*—1 to 4 pills 2 gr

**Tabellæ Quininae (B P C)** contain 1 gr (0.06 g) of quinine sulphate

**Tablets Ammoniated Quinine Compound**, each equivalent to ammoniated solution of quinine  $\frac{1}{2}$  dr, capsicum  $\frac{1}{10}$  gr, camphor  $\frac{1}{10}$  gr, caffeine citrate  $\frac{1}{2}$  gr, aloin  $\frac{1}{10}$  gr Serviceable in influenza

**Tablets Quinine Acid Sulphate** 1 gr with camphor  $\frac{1}{2}$  gr, also this combination with **[P1 S1] Aconite Tincture** 1 m

**[P1] Rhinitis Tablets (Parke, Davis, London)** Powdered camphor  $\frac{1}{2}$  gr, quinine sulphate  $\frac{1}{2}$  gr, fluid extract of belladonna root  $\frac{1}{2}$  m in each tablet *Dose*—1 to 4

**Quininae Tannas (B P, P Helv. V, P G VI, P Ned V, P Ital V, P. Jap)**

*Dose*— $1\frac{1}{2}$  to 15 grains (0.1 to 1 g)

An amorphous yellowish-white powder, obtained by the decomposition of the sulphate with a solution of tannin

**Soluble** slightly in water and about 1 in 3 of alcohol 90%

Being almost tasteless it is recommended for children, to be given in milk, but the slow dissociation in the intestines may be a disadvantage.

**Tabellæ Quininae Tannatis.** Contain 1 grain in a chocolate basis Suitable for children As a prophylactic of malaria Have also been given for whooping cough and as a stimulant in entero-colitis in children

**Quininae Valerianas (B.P.C.).** (Termed "basic" in *Fr. C* and *P. Ital. V*).  $C_{20}H_{24}O_5N_2, C_4H_9, COOH, H_2O - 444.3$

*Dose*—1 to 3 grains (0.06 to 0.2 g.).

White crystals, or powder with slight valerianic odour Contains not less than 71% of anhydrous quinine

**Soluble** 1 in 120 of water, 1 in 2 of alcohol 90%.



**Pilulæ Ferri Valerianatis Compositæ (B.P.C.).**

*Syn.* PILULÆ TRIUM VALERIANATUM.

*Dose.*—1 or 2 pills. Contain 1 gr. each of the valerianates of iron, quinine and zinc. For nervous headache and hysteria. Have been found of value in paroxysmal sneezing.

**Cinchona Febrifuge.**

Originally this product consisted of the mixed alkaloids from *C. succirubra*. Owing to the cultivation of other species and of hybrids yielding more quinine, cinchona febrifuge has become a very variable product. For analyses of different samples, see J. A. Goodson and T. A. Henry, *Quart J. Pharm.*, 1930, 238.

In recent years *C. Ledgeriana* has been encouraged (to increase quinine production) at the expense of the other alkaloids. Recent samples of cinchona febrifuge suggest they have been made from *C. Ledgeriana* after the extraction of the quinine, and they contained greater amounts of amorphous alkaloids and quinidine. Although it is believed that cinchona alkaloids have equal anti-malarial action, it is important to have a definite standard—*Brit med J.*, 1/1930, 27.

The following formula is said to be superior to any other in prophylaxis and superior to quinine in chronic cases of malaria fever as a remedial measure. Powdered cinchona febrifuge 10 gr., citric acid 20 gr., magnesium sulphate 20 gr., spirit of anise 10 m., syrup to  $\frac{1}{2}$  oz. *Dose*— $\frac{1}{2}$  ounce 2 hours after meals—T. H. Bishop, *Indian med Gaz.*, 1924, 644, *ibid.*, 1925, 193.

Benign tertian malaria well treated with a similar mixture. Cheap and suitable for mass treatment—O. A. R. Berkeley-Hill, *Indian med Gaz.*, 1926, 333.

Cinchona febrifuge has never attained any great popularity in India, and its consumption is on the decline—*Brit med J.*, 1/1933, 923.

**Quinetum (B.P.C.).**

*Dose.*—1 to 10 grains (0.06 to 0.6 g.).

As defined by the Malaria Commission of the League of Nations in 1931, it consists of a mixture of equal parts of quinine, cinchonidine and cinchonine, thus corresponding approximately to the relative proportions of these alkaloids in the total alkaloids of red cinchona bark. It is more constant in composition than cinchona febrifuge.

**Totaquina (B.P.).**

*Dose.*—1 to 10 grains (0.06 to 0.6 g.).

A nearly white, pale yellowish-grey, or pale brown powder consisting of a mixture of alkaloids. It contains not less than 70% of crystallisable cinchona alkaloids, of which not less than one-fifth is quinine.

**Soluble** almost completely in warm alcohol 95% and in chloroform; partially soluble in ether, benzene and light petroleum, almost insoluble in water.

Field trials carried out under the auspices of the Health Organisation of the League of Nations in Roumania, Nanking, Kuala Lumpur, and other places, show that totaquina acts like quinine as a potent remedy in all forms of malaria. As this was not a carefully controlled experiment, however, it is not possible to decide from it whether totaquina is a little better than quinine or not quite so good. Two types of totaquina were used in the tests, Type I, made direct from the bark of *C. succirubra*, and Type II, made from

residues of quinine extraction and adjusted to the Malaria Commission's standard specification. The observations made at the different centres were not sufficiently precise and unanimous to warrant a final decision on the relative merits of the different samples.—E. J. Pampana and William Fletcher, *Quart. Bull., Hlth Org., L. o. N.*, Sept., 1934.

The Malaria Commission, as a result of these experiments and Dr Fletcher's Report, considered that "Totaquina seems able to fulfil the purpose for which it was intended, since, having regard to its efficacy—equal to or only slightly less than that of quinine—facility of preparation and cost price, its use would enable malaria treatment to be extended over a wider field"—*Quart Bull Hlth Org., L. o. N.*, Sept., 1934

Adult male prisoners in Lahore who were suffering from malaria were treated with quinine and totaquina, types I and II, in strict rotation, according to the method recommended by the League of Nations. In benign and malignant tertian malaria there was no distinct difference in efficacy between quinine and the two types of totaquina in causing the disappearance of parasites and fever. The evidence as to toxicity was not very reliable. It failed to show any significant difference in toxicity between quinine and the two types of totaquina.—E. P. Hicks and S. D. Chand, *Indian med Gaz.*, 1935, 579

From clinical tests, using an experimental batch of Philippine totaquina in doses of 0.6 g three times daily, it is concluded that the combination is about equal to quinine sulphate in its therapeutic effect. It does not destroy the crescents of subtertian malaria, being similar in this respect to quinine and Atebrin, but schizonts and gametocytes of benign tertian disappear in two to three days. Addition of Plasmoquine to the treatment clears the blood of crescents. No untoward effects were observed.—Marañon, Perez and Russell, *Philipp J Sci.*, 1935, 56, 231

**Quinoidine** Dose—2 to 4 grains (0.12 to 0.25 g) thrice daily

The name given to a mixture of alkaloids (discovered by Seturner, 1830) in the mother liquor after the crystalline alkaloids have been separated. It occurs generally as a dark treacly compound or as a hard mass, and has been stated to be of greater value than salts of quinine. Benign tertian cases required 9 to 13½ gr of quinoidine to stop fever, malignant tertians required an average quantity of 10 to 16 and quartan cases an average of 22 to 24 gr

[P1 81] **Laverain Tablets.** Dose—Up to 6 or 12 during the day

Contain quinoidine 2 gr, ammonium picrate ½ gr, and arsenious acid ⅓ gr. The picrate is employed as an anti-malarial drug in addition to the quinoidine. The arsenic acts as tonic. The preparation is said to be prompt in reducing malarial fever, and good in prophylaxis. A preliminary purge to be given—See D. G. Marshall, *Lancet*, 11/1918, 417

**Plasmoquine Simplex** (Bayer Products, London)

Syn. PLASMOCHIN (Bayer Products, London), BEPROCHIN

$C_{19}H_{29}ON_3 = 315.3$

N-Diethylaminoisopentyl-8-amino-6-methoxyquinoline, a synthetic antimalarial slightly soluble in water, available in tablets containing 0.01 g. and 0.02 g. Except for blackwater fever, in quinine idiosyncrasy, or when quinine is contraindicated, it is best given as—

**Quino-Plasmoquine**, tablets of which contain plasmoquine 0.01 g. and quinine sulphate 0.3 g.

The following scheme of dosage and treatment is now advised, 1st week, 7 days 2 tablets thrice daily; then a further 4 weeks' treatment (with 4 days interval between each week) of 12 tablets daily. In subtertian malaria the first period should be 5 days,

followed by 4 days break, and the subsequent 5 courses of 5 days each instead of 7.

Does not replace quinine, but affords an alternative treatment in patients unable to take quinine. Occasional signs of relative intolerance are slight cyanosis, dyspepsia, colic, and splenic pain—P. Manson-Bahr, *Lancet*, ii/1928, 497.

No one should take Plasmoquine who is not under close daily medical supervision. It cannot replace quinine in the mass treatment of malaria—*Lancet*, ii/1929, 834.

An effective prophylactic against malarial infection—S. P. James, W. D. Nicol and P. G. Shute, *Lancet*, ii/1931, 342. See also P. Manson-Bahr, *ibid*, 425. A review of recent experiences.—*Ibid*, 535.

In malignant tertian malaria not more effective in preventing relapses than quinine. A drug needed with the same action but less toxic and which would not only cure attacks, but prevent relapses. Before attributing remarkable curative properties to a new anti-malarial, one should ascertain whether cases could not be as easily cured with moderately small doses of quinine—Col. S. P. James, *Brit. med. J.*, i/1932, 101. Plasmoquine highly specific for *Plasmodium vivax* but much less so for the merozoites of the subtertian. Of value in pregnancy and in the convalescent stages of blackwater fever. There is undoubtedly idiosyncrasy to it as to quinine.—P. H. Manson-Bahr, *ibid*.

Appears to be well tolerated by pregnant women—P. Manson-Bahr, *Lancet*, i/1932, 883.

Plasmoquine assists malariologists as follows: (1) In minute doses given to gametocyte carriers prevents infection of mosquitoes. (2) In dose of 0.06 g spread over a week it removes gametocytes from the blood. (3) In somewhat larger doses it prevents infection after injection of sporozoites. (4) In 2 treatments (0.06 g. over a week) it prevents relapses, reduces number of carriers, and so reduces number of infections.

Badly infected estates in Ceylon in which antilarval measures were impossible kept practically free from malaria for more than two years by anti-gametocyte dosing with Plasmoquine—Lt-Col. W. W. Clemesha, *Lancet*, i/1932, 750.

In a group of 46 patients treated with Plasmoquine, boys of 12 receiving 0.01 g. and younger boys half this dose, the incidence of malignant tertian infection was 35% compared with 11% among those untreated. In 35 cases of malignant tertian malaria and 13 cases of the benign type in which 1.2 g. of Atebrin in a four-day course was the only treatment, there was a maximum of 5 and 2 relapses respectively during two months—L. E. Napier, D. Butcher and C. R. D. Gupta, *Indian med. Gaz.*, 1932, 186.

There is no satisfactory drug in existence which, taken in therapeutic doses, will prevent contraction of malaria after bites from infected mosquitoes. Plasmoquine in maximum therapeutic doses can be tolerated for 8 days or more and has the same effect as a true causal prophylactic should have, but as the prophylactic dose is too near the toxic dose to be safely taken for more than a few days it is of little value in the prevention of malaria. Plasmoquine, either alone or in combination with quinine, is not recommended for the treatment of malaria. Small doses (0.02 g.) have little or no curative action on asexual forms of the malarial parasites and daily doses of 0.06 to 0.08 g. may cause cyanosis, fatigue, profuse perspiration, or cardiac symptoms.—Col. S. P. James, Health Organisation of the League of Nations, *Brit. med. J.*, ii/1933, 928.

It is admitted that, with a daily dosage of 0.06 g. or over, toxic symptoms are of common occurrence, but with the smaller doses which are in common use for the routine treatment of malaria, e.g., 0.015 g., severe toxic complications are of comparatively rare occurrence. Unable to agree with the findings of the Malaria Commission that the combined quinine and Plasmoquine treatment for benign tertian malaria is "of doubtful value." If one is to condemn the use of this valuable drug, Plasmoquine, because of a relatively small number of cases of serious results often due to improper individual dosage or supervision, one should equally condemn many of the new arsenical preparations used in the treatment of syphilis and other diseases.—J. A. Sinton, *Quart. Bull. Hlth. Org.*, L. O. N., 1935, 657.

The prophylactic value of quinine rather doubted by Army experts; evidence in favour of Plasmoquine obtained, but lower doses ineffective and toxicity of higher doses led to doubts as to use on large scale. As a therapeutic agent, however, it established its position during 1932, the average relapse rate during

1927-31 being 277 per 1000 and for 1932 in Plasmoquine-treated patients 20 to 47 per 1000—Army Health Rept. 1932, *Brit. med. J.*, 1/1934, 253.

**Atebrin** (*Bayer Products, London*). Dihydrochloride of 2-methoxy-6-chloro-9- $\alpha$ -diethylamino- $\delta$ -pentylaminoacridine. A yellowish powder with a bitter taste soluble in water, giving a neutral solution. Available in 0.1 g tablets. *Dose*.—Children up to 4, 1 tablet daily, children from 4 to 8, 2 daily; adults and children over 8, 3 daily. Taken after meals. Course lasts 4 to 7 days.

The advantages claimed for Atebrin are that its action is prompt, it is easy and pleasant to take with no disquieting accompaniments, its toxicity is low, it is freely soluble, it prevents relapses, and can safely be used in complicated forms of malaria, as when hæmoglobinuria or coma is present. Over 300 patients treated with uniformly gratifying results—United Fruit Company Report, 1931, *Brit. med. J.*, 11/1932, 642.

In a daily dose of 1 tablet (0.1 g) is effective as a clinical prophylactic but cannot ordinarily be used for the purpose as even this small dose quickly colours the skin yellow. It is, however, as efficient as quinine in the control of malarial paroxysms, and in cases with severe vomiting or other malignant symptoms, may be given intravenously or intramuscularly, a suitable dose intravenously being 0.3 g. in 5 ml. normal saline—Col. S. P. James, Health Organisation of the League of Nations, *Brit. med. J.*, 11/1933, 928.

**Treatment of malaria in Europeans—49 cases** Definitely superior to quinine in treatment, is well tolerated by children, and invaluable in cases with idiosyncrasy to quinine. A high percentage of Europeans develop yellow discoloration of the skin. Atebrin by itself is relatively non-toxic but has cumulative action and is excreted slowly, thus toxic symptoms may not appear till some time after treatment has ended. Signs of toxicity observed in Europeans were headache in one case and abdominal pain (responding to diet and alkalis) in 12% of cases. A combination of Atebrin and Plasmoquine more toxic than Atebrin alone and should never be used in the febrile stage of subtertian malaria. Relapse rate reduced from 60 to 43%, and treatment beyond 5 days probably does not lessen tendency to relapse, 1.5 g being the optimum adult dose—P. D. Johnson, *Brit. med. J.*, 1/1934, 473. See also E. J. R. MacMahon, *ibid*, 477.

The treatment of malaria is short, simple and economical. Most sufferers appear to be cured within a week. It is not unpleasant to take, is not depressing and is well tolerated even by pregnant women and young children and in black-water fever. Relapses are rare, those treated with it are rid of the infection and are completely non-infective to their fellows. In subtertian malaria it is necessary to give a 5-days course of Plasmoquine in addition. Results so favourable that Atebrin and not quinine is now the drug in ordinary use for the treatment of malaria on estates served by the Malacca Agricultural Medical Board (Straits Settlements)—A. L. Hoops, *Brit. med. J.*, 1/1933, 993.

During the malaria epidemic in Ceylon it was noted that patients who were given Atebrin (0.1 g. thrice daily) on admission took, on an average, at least three days to come to normal, while those given quinine bisulphate 7½ gr. in a mixture thrice daily took, on an average, from 1½ to 2 days. With regard to subsequent attacks, a 5 day's course of Atebrin was found to keep patients free from symptoms of malaria for a much longer period than the short courses of 5 to 7 days of quinine. Patients returning with fever after a course of Atebrin were more seriously ill and it took longer to bring their temperature to normal. Toxic effects with Atebrin not uncommon. It frequently caused epigastric pain, and symptoms of mental derangement lasting two or three days occurred in a fair number of cases towards the end of a course of treatment or shortly after its completion. In children, Atebrin by the mouth caused vomiting and diarrhoea—S. Somasundram, *Trans. R. Soc. trop. Med. Hyg.*, 1935, 103.

To-day it is justifiable to regard Atebrin as an anti-schizont remedy the value of which has been established in practice and with which a successful course of treatment can be carried out in a remarkable short space of time.—F. M. Peter, *Trans. R. Soc. trop. Med. Hyg.*, 1935, 50.

The advantages of Atebrin in the treatment of malaria amongst controlled labour forces in Malaya. While the total drug treatment with Atebrin actually costs less than with quinine in properly supervised cases, there is a still greater saving effected by the low relapse rate, lessened absence from work and the greater efficiency; the shortness and simplicity of administration is a further point

in its favour. Atebrin is the best drug available for the controlled treatment of all types of malaria in Malaya, where effective oral administration is preferable to injection.—A. L. Hoops, *Trans. R. Soc. trop. Med. Hyg.*, 1935, 249

Mass treatment with Atebrin was given to labour forces on several malarial areas in Malaya. On two malarial divisions of different estates it was given in an attempt to prevent the usual seasonal epidemic and was apparently successful. On other malarial areas epidemics were controlled in a few days by an initial intensive treatment and the malaria rate kept low by a "follow-up" treatment given once and twice weekly. Atebrin was given in varying doses for periods up to four months without any apparent ill-effects and without upsetting the labour forces. No serious toxic effects such as mental symptoms were seen amongst the many thousands of coolies treated. A certain number of cases of colic occurred—approximately 3%.—R. B. Wallace, *J. trop. Med. (Hyg.)*, 1936, 39

Atebrin in any form cannot take the place of quinine, which, in the vast majority of cases, is effective in producing a clinical cure, and often a radical cure, especially in mass therapy. From the results obtained in Ceylon by the use of a combination of quinine and Plasmoquine in short courses, and in non-toxic dosage, this would appear to be the best agent to use in mass therapy for all types of parasites, and in all their stages.—C. L. Dunn, *Trans. R. Soc. trop. Med. Hyg.*, 1936, 243

**Atebrin Musonate** (Bayer Products, London) Atebrin for intramuscular or intravenous injection, supplied in dry ampoules containing the water-soluble salt, Atebrin dimethanesulphonate, corresponding to 0.1 or 0.3 g. of Atebrin hydrochloride. To be dissolved when required for use in 3 ml. or 9 to 10 ml. respectively of sterile water. Solutions must not be heated or stored for any length of time. Is best given intramuscularly, dosage being the same as that of Atebrin given orally (*see above*). If given intravenously the single dose of 0.1 g. should not be exceeded and the injection should be given very slowly. Is especially indicated where there is an abnormally large invasion of parasites, and severe complications.

Death following intramuscular injection. It seems difficult to be certain beforehand whether a patient will react badly to Atebrin, and also difficult to increase its excretion once a full therapeutic dose has been injected.—P. B. Ferrando and E. M. Wijerama, *Lancet*, ii/1935, 1056

Among adults, pregnant women have been found particularly liable to collapse after injections. Convulsions due to malaria were of frequent occurrence among children in the early stages of the epidemic. Convulsions occurring a few minutes or hours after an Atebrin injection and attributed to the Atebrin injection have occurred in both children and adults. They were always fatal.—R. Briercliffe, Report on the Malaria Epidemic in Ceylon, per *Lancet*, ii/1935, 1078

Two intramuscular injections of 0.375 g. at an interval of 24 hours brought the temperature down in the majority of cases and caused disappearance of the asexual stages of the parasites (whether *P. vivax* or *P. falciparum*) as a rule within 3 days. Ill-nourished children are likely to collapse shortly after the injection, with vomiting, giddiness and fainting. Unable to arrive at the conclusion that treatment with Atebrin Musonate is in any way superior to that of quinine as regards immediate effects, though the injections are painless.—S. Somasundram, *Trans. R. Soc. trop. med. Hyg.*, 1935, 104

Owing to the very slow excretion or destruction of Atebrin in the body it seems unnecessary to exceed for intravenous injection the dose of 0.1 g., for an adult. The margin of safety is probably not great and intravenous injection should be resorted to only in emergency. The injections should be made very slowly and timed to take several minutes for completion. The total injection over a period of twenty-four hours should not exceed 0.3 g.

Untoward effects of Atebrin appear to include gasping or accelerated respiration, circulatory failure, collapse, vomiting, possibly rise of temperature, psychoses, loss of appetite and of weight, abdominal pain, headache, diarrhoea, yellowed sclera, rather persistent yellowing of the skin.

In view of the very slow excretion or destruction of the drug in the body, it is reasonable to consider that a course of treatment with it should not be repeated

within a period of, say, eight weeks, and that the drug should be taken under supervision of a physician.—W T Dawson, W Gingrich, and E D Hollar, *Amer J trop. Med*, 1935, 15, 515

There were no toxic symptoms following intravenous or intramuscular injection in 34 cases, and inadvertent escape of the solution into the subcutaneous tissues caused no inflammation. As far as can be judged from a small series of cases, Atebrin Musonate is better given intramuscularly, and three daily doses or possibly four appear to be adequate. It may be necessary to revise this opinion if it is found that larger doses can be safely given intravenously. The cost of three intramuscular doses of Atebrin Musonate, 0.375 g. each, is four times that of 1 ounce of quinine or of a course of 15 tablets of Atebrin dihydrochloride. Atebrin Musonate would thus be uneconomical for routine use in natives, but the slight inconvenience involved and lack of all unpleasant toxic symptoms, make it a strong rival to quinine and oral Atebrin for patients able to bear the expense.—J. A Carman and R P Cormack, *Trans R Soc trop Med Hyg*, Jan, 1936, 395.

**Cupreæ Cortex.** The bark of *Remyia pedunculata* and other species. Contains the alkaloid cupreine,  $C_{19}H_{22}O_2N_2 = 312.2$ , which is allied to quinine and also about 2 to 3% of quinine. Cupreine salts have been employed similarly to the salts of quinine. It can be converted into quinine by treating with sodium in methyl alcohol solution and heating the solution with methyl iodide.

Several cupreine derivatives have been used —

**Amylhydrocupreinae Dihydrochloridum**,  $C_{24}H_{44}O_2N_2 \cdot 2HCl$ , is the dihydrochloride of the isoamyl derivative of hydrocupreine. Sparingly soluble in water, readily in alcohol. Suggested as antiseptic and anæsthetic in nose and throat affections, including diphtheria.

**Ethylhydrocupreina.** *Syn and Prop. Name* OPTOCHIN (Howards, Ilford), NUMOQUIN  $C_{21}H_{28}O_2N_2 = 340.2$

*Dose* — 4 grains (0.25 g.) Max dose during the day 15 grains (1 g.) Not to be given on an empty stomach.

A minutely crystalline powder with bitter taste. Almost insoluble in water, soluble in alcohol, ether, chloroform and dilute acids.

It is prepared synthetically from quinine by hydrogenation, demethylation to hydrocupreine and subsequent ethylation.

**Uses.** In pneumonia, treatment should be commenced immediately on diagnosis. Ethylhydrocupreine base is administered in single doses of not more than 3 grains (0.2 g.) every four hours, day and night, the drug should not be administered longer than for three days, so that a total day's dose of 18 grains (1.2 g.), and a total dose for the whole period of 54 grains (3.6 g.) should not be exceeded. A regular milk diet should accompany the medication. If disturbances of vision or hearing occur administration should at once be stopped.

*For children* the dose of the base should be much less—at least a quarter or half the above figures.

The drug has also been given in malaria.

The bacteria in pneumonia are destroyed by ethylhydrocupreine and even the blood drawn from patients so dosed will destroy pneumococci—our only instance of specific drug therapy in acute general bacterial disease.—W E Dixon, *Brit med J.*, 11/1922, 410.

The action of the compound on the pneumococcus and of isooctylhydrocupreine on *B. diphtheria* is absolutely specific, and enough can be given by medicinal doses to clear the blood of these micro-organisms.—W. E. Dixon, *Brit. med. J.*, 1/1925, 814.

Amaraosis following ingestion of a total of 58 grains of ethylhydrocupreine over 3 days —B. Alvis, *J. Amer. med. Ass.*, 11/1929, 1253.

PRIMARY PNEUMONIA in infants well treated by Optochin salicylic acid ester, in the form of suppositories (retained for 10 to 15 minutes). Infants under 1 year receive 0.02 to 0.03 g. three or four times a day, from 1 to 2 years from 0.03 to 0.04 g., from 2 to 5 years 0.04 to 0.05 g., and older children 0.05 to 0.1 g. Must not be given for more than 3 or 4 days and must not be given in presence of inflammation of the kidneys. Forty-five children (half of them under 2 years) treated with only one death. Complications rare.—*Lancet*, 11/1932, 139.

An average mortality of 25% for bronchopneumonia in children contrasted with a consecutive series of 44 cases treated with Optochin without a single death.—*Brit. med. J.*, 1/1933, 968.

PNEUMONIA —Serum therapy is rarely used in Germany but Optochin and Solvochin are widely used there and in America —P. Martini, *Brit. med. J. Epit.*, 1/1933, 68.

**Unguentum Æthylhydrocupreinae** 1% in white soft paraffin; must be freshly made. Efficiency decreases in 3 to 4 days. Used in pneumococcal and gonorrhœal eye affections.

**Æthylhydrocupreinae Hydrochloridum** (*B.P.C.*, *P. Helv. V*, *P. Ned. V*). *Prop. Name.* OPTOCHIN HYDROCHLORIDE (*Howards, Ilford*).  $C_{21}H_{23}O_2N_2.HCl = 376.7$

*Dose.*—No dose is given in *B.P.C.* or *P. Ned. V.*; *P. Helv. V* gives max. single dose 4 gr., max in 24 hours 12 gr. approx. These doses should be given with caution. The base (*antea*) should be employed in pneumonia. The hydrochloride may cause grave visual disturbances owing to more rapid absorption.

A white crystalline powder soluble in water about 1 in 4.

*Uses.* Though given internally in some cases (it has been proved effectual as a prophylactic of common colds), it is mostly used locally in 1 or 2% solution in eye affections especially in pneumococcal infections and as a prophylactic against infection in laceration of the cornea. Its use is at first painful but anæsthesia is produced in 2 to 30 seconds.

Ulcus corneæ serpens has been treated with a 1% ointment (made with the base) or a 1% or 2% solution. A pad of sterile wool or gauze is soaked in the solution and then left on the ulcer for 5 or 10 minutes. After this the 1% solution is instilled into the eye every hour or so during the day, or the ointment applied 5 to 6 times *per diem*. *Note.*—Solutions should be freshly prepared. They decrease in efficiency after 3 or 4 days.

In gonorrhœal conjunctivitis and photophobia accompanying eczematous conjunctivitis, scrofular ophthalmia, and keratitis, has also proved useful.

Pneumococcal meningitis treated by  $\frac{1}{2}$  gr. intraspinal doses together with anti-pneumococcal serum. One case, with Optochin alone, did not respond favourably—referred to by C. Worster-Drought, *Med. Pr.*, 1/1922, 514.

Inhibits pneumococcus in dilution 1 in 1,000,000.—G. T. Langley, *Lancet*, 1/1924, 13.

**Methylhydrocupreinae Hydrochloridum.** *Syn.* HYDROQUININE HYDROCHLORIDE.  $C_{20}H_{26}O_2N_2.HCl.2H_2O = 398.7$ .

*Dose.*—Intravenously, 4 to 12 grains (0.25 to 0.8 g.) for adults—for malaria and trypanosomiasis. For whooping cough in young children up to 6 months,  $\frac{1}{2}$  to  $\frac{3}{4}$  grain (0.02 to 0.05 g.); 6 to 12

months,  $1\frac{1}{2}$  grains (0.1 g.); from 2 to 14 years,  $1\frac{1}{2}$  to 8 grains (0.1 to 0.5 g.) intramuscularly.

**Soluble.** 1 in 8 of water.

**Octylhydrocupreinae Dihydrochloridum** is the isooctyl compound. A 0.5 to 1% solution has been used as a disinfectant for wounds.

**Vuzin** (*Zimmer, Mannheim, Howards, Ilford*). Brand of octylhydrocupreine dihydrochloride. Supplied in tablets containing 0.1 g for preparation of an antiseptic wound solution

**Peganum** (*B.P.C.*). The dried seeds of *P. Harmala* (*Rutaceae*). Contains the alkaloids harmaline, harmine and harmalol.

**Banisterine** from *Banisteria Caapi* is an alkaloid identical chemically and pharmacologically with harmine

Harmaline has a toxic action on trypanosomes *in vitro*, but no curative effect on the disease in man. It is thought inferior to quinine for acute malaria. Harmine failed to cut short acute attacks. In three cases of relapsing fever it proved remarkably successful.

Trypanosomiasis treated by harmala alkaloids (Gunn)—not found curative. Review of tropical diseases—R. Hewlett, *Practitioner*, April, 1921

Harmine has been used in parkinsonism. Harmaline and harmine were tried in malaria—J. A. Gunn, *Lancet*, 1/1929, 769

Harmine 0.04 g hypodermically thrice daily useless in parkinsonism causes toxic symptoms—T. R. Hill and C. Worster-Drought, *Lancet*, 11/1929, 647, 675

Harmine—a therapeutic revival—*Per Prescriber*, 1/1929, 225; see also *ibid*, 11/1929, 312

Harmalol is only 1% soluble in cold water. Harmalol hydrochloride in doses of  $\frac{1}{2}$  gr hypodermically or by mouth has slight but definite effect in relieving muscular rigidity in parkinsonism, but has no effect on the tremor or mental condition and does not relieve salivation. Not so good as hyoscine, but of value as an adjuvant—H. A. Cooper and J. A. Gunn, *Lancet*, 11/1931, 902

Recent pharmacological studies suggest harmol as one of the most powerful coronary dilators, 1 in 200,000 having marked effect on rabbits. Suggested for clinical trial in angina pectoris—J. A. Gunn and R. C. MacKeith, *Quart J Pharm*, 1931, 33.

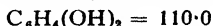
**Picrorrhiza** (*B.P.C.*) *Dose*—10 to 60 grains (0.6 to 4 g.) The dried rhizome of *P. Kurroa* (*Scrophulariaceae*). Tonic, antiperiodic, aperient. This and *Amphucome Emodi* are called Kaur. Inferior to quinine—I.D.C.

**Extractum Picrorrhizae Liquidum.** *Dose.*—15 to 60 minims 1 in 1 of alcohol 60%

**Tinctura Picrorrhizae.** *Dose*— $\frac{1}{2}$  to 1 drachm 1 in 4 of alcohol 45%

## RESORCINOL

*B.P., U.S.P. XI, P. Helv. V, P. Dan., P. Ital. V, P. Belg. IV, F.E. VIII (for external use).*



*Syn.* RESORCINUM, RESORCIN, *m*-DIHYDROXYBENZENE

*Dose.*—1 to 5 grains (0.06 to 0.3 g.). *U.S.P. XI* average dose 2 grains.

White crystalline plates or powder, melting at  $110^\circ$  to  $111^\circ$ , and easily volatilised. Preserve from light.

**Soluble** 1 in 1 of water, 1 in 1 of alcohol 90%, 1 in 20 of olive



oil, 1 in 1 of ether, 1 in 1 of glycerin, very slightly soluble in chloroform, carbon disulphide and benzene.

**Incompatible** with spirit of nitrous ether and caustic alkalis.

**Uses.** Resorcinol has useful antiseptic properties. It coagulates protein, and has a caustic action on the skin, but a 2% solution is not irritating. A 5% solution may be injected into the bladder, without causing any irritation, in inflammatory affections of this organ, likewise in vesical catarrh after gonorrhœa; 5 to 10% solution is of service also in syphilitic sores and skin diseases. A 1% solution is useful as an eye lotion in conjunctivitis. Given internally, *but with great care*, it has been used as an antipyretic but it cannot be recommended. In whooping cough and hay-fever, 10 minims of 2% solution, or this strength used as spray, is of service. Epithelioma and rodent ulcer have been treated with ointments and plaster up to 30% strength. It is applied locally to condylomata and mucous patches. A pigment of 10% relieves irritation of tubercle of larynx. For eczema and alopecia, cold cream with 2% of resorcinol is useful. Stimulating hair lotions frequently contain resorcinol. In using these it is important to free the hair from soap and alkali, otherwise the hair may be discoloured. In the form of paste it has proved useful in ichthyosis—favours desquamation and removes effete horny layer. In gastric ulcer 2 to 5-grain doses have antiseptic action.

Resorcinol is dangerous when applied over large surfaces. A paste containing 25 to 30% resorcin in gelanthum proved fatal.

**Gargarisma Resorcini** (*PEHC.*)

Resorcinol 15 grains, glycerin 1 dr, water to 1 oz

**Glycerinum Resorcini** (*GH.*)

Resorcin 4, distilled water 4, glycerin to 15.

In chronic urethritis resisting treatment, a single injection has been found beneficial.

**Gutt. Auribus Resorcinol.** (*NIF*) Resorcinol 5 gr, industrial methylated spirit 6 dr., water to 1 oz.

**Lotio Capillaris.** Resorcinol 5, capsicum tincture 15, otto of rose *qs*, castor oil 10, alcohol 90% to 100. A stimulant to the growth of hair.

[P1] **Lotio Excitans** (*St GH*). Resorcinol 5 gr, mercuric chloride  $\frac{1}{2}$  gr, glacial acetic acid 3 m, chloral hydrate 10 gr, tincture of cantharides 20 m, alcohol 60% to 1 oz. For the scalp.

[P2] **Lotio Resorcinolis Composita** (*Mid H*). Resorcinol 5 gr, mercuric chloride  $\frac{1}{2}$  gr, castor oil 15 m, tincture of quillaia 7  $\frac{1}{2}$  m, spirit of rosemary 30 m, mucilage of tragacanth 15 m, water to 1 oz. A stimulating application for pityriasis of the scalp. *St M H* has resorcinol 10 gr, industrial methylated spirit 1 dr, water to 1 oz.

**Lotio Resorcinolis et Acidi Borici.**

Resorcinol 1, compound tincture of lavender 10, glycerin 10, saturated solution of boric acid 80. A mouth-wash.

**Lotio Resorcinolis et Acidi Salicylici.**

Salicylic acid 30 gr, resorcinol 1 dr, spirit of rosemary 1 oz, saponin 1 dr., lanolin 1 oz., Aqua Mellis to 10 oz. Dissolve the salicylic acid and resorcinol in the spirit of rosemary, melt the lanolin, add the saponin dissolved in a little water, place in a warmed mortar, add the resorcinol solution and the Aqua Mellis in parts to make a cream.

[P1] **Lotio Resorcinolis Pilocarpinæ et Cantharidini.**

Resorcinol 80 gr, pilocarpine hydrochloride 15 gr, solution of cantharidin 1  $\frac{1}{2}$  oz., tincture of capsicum 4 dr, spirit of camphor 6 dr, castor oil 10 to 60 m, oil of lavender 30 m, alcohol 90% to 8 oz. A useful stimulating lotion in alopecia prematura for use after exfoliative treatment.

**Nebula Resorcinollis.** For a cold, spray nostrils with 1% solution.

**Pasta Resorcinolis (B.P.C.).** *Syn.* LASSAR'S STRONGER RESORCIN PASTE.

Resorcinol, zinc oxide and starch, of each about 20% with liquid paraffin.

**Pasta Resorcinolis Mitis (B.P.C.).** *Syn.* LASSAR'S MILD RESORCIN PASTE.

Resorcinol about 10%, zinc oxide and starch, of each about 25%, with liquid paraffin.

**Spiritus Resorcinolis (B.P.C.).** *Syn.* LOTIO RESORCINOLIS COMPOSITUS, SPIRITUS CAPILLARIS.

Resorcinol and castor oil of each 1 in 40 in Cologne spirit and alcohol.

Useful for dandruff and alopecia.

**Unguentum Resorcinolis (B.P.C.).** 12½% in glycerin, wool fat and white soft paraffin. *R.L.O.H.* has resorcinol 4 gr., yellow soft paraffin to 1 oz.

**Unguentum Resorcinolis Compositum (B.P.C.).** Resorcinol 4%, bismuth subnitrate 8%, with water, starch, zinc oxide, birch tar oil and potassium pyrosulphite in wool fat, ceresin and yellow soft paraffin.

**Unguentum Resorcinolis Compositum (St. J.H.).** *Syn.* IHLE'S PASTE. Resorcinol, zinc oxide, starch, of each 22 gr. in soft paraffin to 480 gr.

Has been used stronger for bromide acne

Resorcin liquefies with menthol, camphor or phenol, and a small amount of any of these may well be added so as to form a uniform ointment

**Unguentum Resorcinolis et Acidi Salicylici.** *Syn.* CASTELLANI'S OINTMENT. Resorcinol 60 gr., salicylic acid 10 gr., lanolin and soft paraffin to 1 oz

The most popular remedy for Dhobie itch in Africa and Asia.

**Unguentum Resorcinolis et Bismuthi Compositum (B.P.C.).** Resorcinol and bismuth subchloride of each 8%, with water, zinc oxide, starch, birch tar oil, oil of cade, and wool fat.

**Ruscoln (Evans, Sons, Lescher & Webb, Liverpool)** Ointment containing resorcinol, oil of cade, zinc oxide, etc., in a lanolin base. Eczema, hæmorrhoids, etc

**Resorcinolis Monoacetatis.** *Syn. and Prop. Name.* RESORCIN MONACETATE, EURESOL (*Knoll, Ludwigshafen; Pharmaceutical Products, London*).

Mix resorcinol 440 and acetyl chloride 320 and allow to interact completely in an open dish. Then heat to 100° for ½ hour. Cool, wash free from acid with water, and dry over exsiccated sodium carbonate.

A reddish-yellow, viscous liquid. Dissolves 10 to 30% in acetone, for use in acne, seborrhœa and syphilis. Euresol pro Capillis has perfume added. Removes dandruff and itching.

**Lotio Resorcinol Monoacetatis Compositum (B.V.H.).** Solution of resorcinol monoacetate (1 in 2 in acetone) 2 dr, solution of formic acid (25%) 10 m, spirit of rosemary 1 dr, sodium taurocholate 2 gr, water to 6 oz

**Thio-resorcinol.** Yellowish powder slightly soluble in alcohol, as a substitute for iodoform, 5% ointment in skin diseases

**Hexyl-Resorcinol (B.P.C.).**  $C_6H_3(OH)_2 \cdot (CH_2)_5 \cdot CH_3 = 194.1$ .  
*Syn.* 1 : 3-DIHYDROXY-4-HEXYLBENZENE.

*Dose.*—2 to 10 grains (0.12 to 0.6 g.) thrice daily.

Gelatin capsules containing 0.15 g. in 25% olive oil solution are taken *immediately after* each meal thrice daily, 3 to 4 being taken on each occasion; they must not be taken on an empty stomach. *B. coli* infection may need 60 to 90 days' continuous treatment.

**Patents.** The manufacture of hexyl-resorcinol and allied compounds is covered by a number of British patents dating from 1923, owned by American manufacturers. In 1927 they were the subject of an action in the Courts. Details in 19th Edn., p. 753.

Stable white crystals with pungent odour and astringent taste, m.p. not below  $66^\circ$ .

**Soluble** 1 in 2000 of water, readily in ether, chloroform and alcohol and in oils.

**Uses.** A powerful germicide, especially for gram-positive organisms, the phenol coefficient ranging from 46 to 52. Its power is retained in both acid and alkaline urine even in high dilution. Given by the mouth, the compound is secreted in the urine at a rate producing continuous action in the urinary tract. Chronic *B. coli* infections and *Staphylococcus* infections have been treated with it; it acts best in early cases. Pyelitis and cystitis caused by organisms other than *B. coli* are cleared up in a few weeks. *B. coli* infections require, on the average, about as many months. It is also of value in tuberculosis of the urinary tract. Continue treatment until sterility of the urine has persisted for a fortnight at least. Externally, a solution of hexyl-resorcinol 1 in a mixture of glycerin 300 and water 700 is used as a disinfectant for the skin and mucous membrane.

In the preliminary experiments a total of 45 g. produced no toxic symptoms, but since then much larger amounts have been given without toxic effects. Urinary tract infections due to *Staphylococcus albus*, *Staphylococcus aureus*, *Streptococci*, some strains of *B. pyocyaneus* and *B. coli* have been cleared up with hexyl-resorcinol alone by mouth—V. Leonard, *J. Amer. med. Ass.*, Dec. 20, 1924.

The bactericidal power is probably due to its being a powerful surface tension reductant. Hence administration of sodium bicarbonate is contraindicated and excessive intake of fluids must be avoided, as they both increase the surface tension of the urine and rob the compound of bactericidal action. So far as is known, nephritis is not a contraindication. Children seem to tolerate relatively larger doses than adults—V. Leonard and A. Wood, *J. Amer. med. Ass.*, 11/1925, 1855.

**ANTHELMINTIC EFFECT** (hookworm, trichinus and ascaris) stated to be good, but unlikely to displace other drugs owing to the need for strict and intelligent co-operation of patient—*Lancet*, 11/1931, 33.

Possibly the most effective substance known against ascaris, well over 90% being removed in over 1000 cases. Its disadvantages are that it combines with protein and is relatively ineffective if taken when food is present in the stomach or intestines, that it causes a certain amount of irritation in the stomach, and that the crystals, unless protected in some way, may cause local "burns" of the mucous membrane of the mouth—it is best given in sugar-coated pills, with instructions that they should not be chewed.—P. D. Lamson and co-workers, *J. Amer. med. Ass.*, 11/1932, 294.

**HOOKWORM.** No attempt has been traced at evaluation of hexyl-resorcinol through deworming. The drug has hitherto caused no deaths. Relative success

depends on starvation, rigorous to a degree required for no other anthelmintic. Encapsulation of the drug shifts to the invisible stomach the ugly necrosis it causes, but æsthetic gain need be no more than a decent shrouding of pathological damage. Hope of its usefulness on a mass scale is slight—C. Lane, *Lancet*, 1/1935, 1463.

**PYELITIS.** Successful in only 1 case out of 14.—Per J. *Amer. med. Ass.*, 1/1926, 1506.

**PELONEPHRITIS, CHRONIC** Improved symptoms and reduced pus in urine, but did not eradicate infection—W. F. Braasch and E. P. Cathcart, *J. Amer. med. Ass.*, 1/1927, 1632.

About one-third of cases cured, with an additional 20% of symptomatic cures about 43% will be improved, and 25% remain unchanged. Coccus infections respond more certainly than bacillus or mixed infections. A higher proportion of cures is likely if the treatment were combined with other methods. Details of treatment of 82 cases of acute and chronic pyelitis and prostatitis—C. W. Eberbach and R. D. Arn, *J. Amer. med. Ass.*, Aug. 14, 1927, 514.

**TISSUE DISINFECTANT** Hexyl-resorcinol is claimed to be effective when 0.1 g is dissolved in glycerin 30 and water 70 ml, and pathogenic micro-organisms are stated to be destroyed in less than 15 seconds. Undiluted the solution may be used for lavage of the urethra, bladder and buccal mucous membranes, and mixed with 2 vols of water it may be instilled into the normal conjunctival sac—*Brit. med. J. Epit*, 11/1927, 100.

**Emulsio Hexyl-Resorcini** (*Gt. Orn. H*) (Dose for 1 year old child.)

Hexyl-resorcinol 1 gr, olive oil 10 m, acacia 2½ gr, chloroform water to 1 drachm.

**Caprokol** (*British Drug Houses, London, Sharp & Dohme, London*) is a solution of hexyl-resorcinol in olive oil. In capsules containing 0.15 g of hexyl-resorcinol or as a 2½% solution.

**Hexylresorcinol Solution S.T. 37** (*Sharp & Dohme, London*) A solution of hexyl-resorcinol of low surface tension (37 dynes per sq. cm) and high bactericidal activity. Used undiluted for cuts, infected wounds, abscesses, etc., and diluted with 1 to 3 parts of water as a mouthwash or gargle.

**Prentif Suppositories** (*Prentif Ltd., London*). Contraceptive suppositories in which hexyl-resorcinol is the spermicidal ingredient in an acid gelatin base of pH 2.2. **Prenols** are the same, but smaller, for use with a cervical cap.

## RHEUM

*B.P., U.S.P. XI, P. Helv. V, P. Dan.*

*Syn. RHEI RHIZOMA, TODAIWO (P. Jap. IV).*

*Dose*—3 to 15 grains (0.2 to 1 g).

The rhizome (*U.S.P. XI*, rhizome and roots) of *Rheum palmatum* and possibly other species of *Rheum* (Polygonaceæ) grown in China and Tibet, partially decorticated and dried.

**Uses.** Laxative and stomachic in atonic dyspepsia. Useful in diarrhœa, since tannin present exerts an astringent action after purgation has effected removal of irritant substance.

A mixture consisting of compound rhubarb powder 1 oz. (sometimes 2 oz.) and chloroform water to 2 oz. causes rapid disappearance of symptoms in bacillary dysentery in children, but is of no use in adults. *Dose*.—1 teaspoonful every 2 hours for a child of 2 years.

**ACUTE BACILLARY DYSENTERY.** Rhubarb ½ teaspoonful of powder in cachets every 1, 2 or 3 hours, until the rhubarb appears in the stools. Stated to be magical.—R. W. Burkett, *Lancet*, 11/1921, 254

**Extractum Rhei (B.P.C.)***Dose.*—2 to 8 grains (0.12 to 0.5 g.).

A dry extract prepared with alcohol 60%.

**Extractum Rhei (U.S.P. XI).** *Average dose.*—8 grains (0.5 g.)

1 g. represents 2 g. of rhubarb.

**Extractum Rhei Liquidum (B.P.C.).***Dose.*—10 to 30 minims (0.6 to 2 ml.). 1 in 1.**Infusum Rhei Concentratum (B.P.C.).***Dose.*— $\frac{1}{2}$  to 1 drachm (2 to 4 ml.). 1 in 2 $\frac{1}{2}$ .

Is 8 times the strength of the fresh infusion.

**Infusum Rhei Recens (B.P.C.).***Dose.*— $\frac{1}{2}$  to 1 ounce (15 to 30 ml.) 1 in 20.**Liquor Rhei Dulcis (B.P.C.)** *Syn.* ELIXIR RHEI*Dose.*—1 to 3 drachms (4 to 12 ml.).A flavoured preparation containing 25% *v/v* of liquid extract of rhubarb.**Mist. Gent. c. Rho** (*N.I.F.*). Sodium bicarbonate 10 gr., concentrated infusion of rhubarb 15 m., concentrated compound infusion of gentian 15 m., peppermint water to  $\frac{1}{2}$  oz**Mist. Rhei Ammon. c. Soda** (*N.I.F.*). Powdered rhubarb 4 gr., sodium bicarbonate 15 gr., ammonium carbonate 3 gr., peppermint water to  $\frac{1}{2}$  oz**Mist. Rhei Co.** (*N.I.F.*) Powdered rhubarb 3 gr., light magnesium carbonate 10 gr., powdered ginger 4 gr., sodium bicarbonate 10 gr., chloroform water to  $\frac{1}{2}$  oz.**Mistura Rhei et Cascarae (B.P.C.)***Dose.*— $\frac{1}{2}$  to 1 ounce (15 to 30 ml.).

Contains rhubarb 4 gr., sodium bicarbonate 12 gr., liquid extract of cascara sagrada 20 m., with liquid extract of liquorice, syrup of ginger and oil of peppermint in chloroform water to 1 oz

**Mistura Rhei et Sodii Bicarbonatis (B.P.C.)** *Syn.* MISTURA RHEI COMPOSITA, MISTURA RHEI ET SODÆ.*Dose.*— $\frac{1}{2}$  to 1 ounce (10 to 30 ml.).

Similar to the preceding mixture but contains no cascara.

**Pilula Rhei Composita (B.P.).***Dose.*—4 to 8 grains (0.25 to 0.5 g.) Contains rhubarb 25%, aloes, myrrh, hard soap, oil of peppermint and syrup of liquid glucose.**Pilulae ex Franck.** *Syn.* PILDORAS DE FRANCK (*FE VIII*).Powdered rhubarb 1 g., powdered aloes 4.5 g., powdered jalap 4.5 g. Mix with a sufficient quantity of syrup and make 100 pills *Dose.*—1 to 3 pills**Pulvis Rhei Compositus (B.P.).** *Syn.* GREGORY'S POWDER.*Dose.*—10 to 60 grains (0.6 to 4 g.)

Rhubarb 25%, with heavy and light magnesium carbonates, and ginger.

**Syrupus Rhei (B.P.C.).***Dose.*— $\frac{1}{2}$  to 2 drachms (2 to 8 ml.)

Liquid extract of rhubarb about 1 in 14, with oil of coriander, in syrup.

**Syrupus Rhei Aromaticus (U.S.P. XI).** *Average dose.*—2 $\frac{1}{2}$  drachms (10 ml.). Aromatic tincture of rhubarb 15, potassium carbonate 0.1, in syrup to 100.

**Tabellæ Rhei et Sodii Bicarbonatis (B.P.C.).** *Syn.* RHUBARB AND SODA TABLETS.

*Dose.*—1 or 2 tablets.

Contain rhubarb 3 gr., sodium bicarbonate  $1\frac{1}{2}$  gr., and ginger  $\frac{1}{2}$  gr.

**Tinctura Rhei Aromatica (U.S.P. XI)** *Average dose.*—60 minims (4 ml.)  
Rhubarb 20, cinnamon 4, clove 4, nutmeg 2, with glycerin, alcohol and water to produce 100.

**Tinctura Rhei Composita (B.P.).**

*Dose.*— $\frac{1}{2}$  to 1 drachm (2 to 4 ml.).

Rhubarb 1 in 10 with cardamom and coriander in a glycerin and alcohol 45% menstruum.

**Sarsa (B.P.C., U.S.P. XI, P. Helv V, P. Dan)** *Syn.* SARSAPARILLA.

The dried root and rootlets of *Smilax ornata* (Liliaceæ). *U.S.P.* includes also other species of *Smilax*. In chronic rheumatism, skin affections and as a "blood purifier," and in syphilis. It was of doubtful value even 150 years ago.

**Decoctum Sarsæ Compositum (B.P.C.)**

*Dose.*—2 to 8 ounces (60 to 240 ml.)

Sarsaparilla 1 in 8, with sassafras root, guaiacum wood, mezereon, liquorice and water

**Decoctum Sarsæ Compositum Concentratum (B.P.C.)**

*Dose.*— $\frac{1}{2}$  to 1 ounce (8 to 30 ml.) Is eight times the strength of the preceding decoction

**Decoctum Zittmanni Fortius.** *Dose.*—3 to 6 ounces

Sarsaparilla (cut small) 200, water 5200, maintain at 35° to 40° for 24 hours, then add potash alum 10, calomel 8, precipitated cinnabar 2. Heat on a water-bath for three hours and add bruised anise and fennel of each 10, senna leaves (cut small) 50, liquorice root (cut small) 20. Continue heating for 15 minutes, strain and press, passing sufficient water through the marc to make up to 5000

**Decoctum Zittmanni Mitius.** *Dose.*—3 to 6 ounces

Sarsaparilla 100, water 5200, lemon peel, cassia bark, cardamom and liquorice of each 6. Proceed as in making the stronger decoction

Both these preparations have been used in syphilis and wasting diseases

**Fluidextractum Sarsaparillæ (U.S.P. XI)**

*Average dose.*—30 minims (2 ml.)

1 ml. represents 1 g. of sarsaparilla.

**Syrupus Sarsaparillæ Compositus (U.S.P. XI)**

*Average dose.*— $\frac{1}{2}$  ounce (15 ml.) Fluidextract of sarsaparilla 20%, with fluidextract of liquorice, oils of sassafras and anise, methyl salicylate, alcohol and syrup.

**Hemidesmus (B.P.C.), syn** INDIAN SARSAPARILLA, is the dried root of *H. indicus* (Asclepiadaceæ), and is used in India as a substitute for sarsaparilla.

**Taraxacum (B.P.C., P. Helv. V).** *Syn.* DANDELION ROOT.

The fresh or dried root of *Taraxacum officinale* (Compositæ). A mildly laxative bitter, without action on the liver.

**Extractum Taraxaci (B.P.C.)**

*Dose.*—5 to 15 grains (0.3 to 1 g.) A soft extract from the juice of the fresh root

**Extractum Taraxaci Liquidum (B.P.C.)**

*Dose.*— $\frac{1}{2}$  to 2 drachms (2 to 8 ml.). 1 in 1

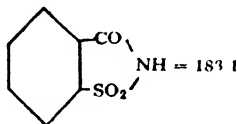
**Succus Taraxaci (B.P.C.).**

*Dose.*—1 to 2 drachms (4 to 8 ml.).

The juice from the fresh root preserved with alcohol

## SACCHARINUM

B.P.C., U.S.P. XI, P. Helv. V, P. Ned. V, F.E. VIII



**Syn. and Prop. Name.** GLUSIDUM, *o*-BENZOIC SULPHINIDE, GLUCUSIMIDE, BENZOYL SULPHONIC IMIDE, BENZOSULPHINIDUM, ORTHOSULFIMIDUM BENZOICUM, IMIDE ORTHOSULFOBENZOIQUE (P. Belg. IV), SAXIN (Burroughs Wellcome, London)

**Dose.**— $\frac{1}{2}$  to 2 grains (0.03 to 0.12 g.) or more. U.S.P. XI average dose  $\frac{1}{2}$  grain.

A white, intensely sweet, crystalline powder. Its aqueous solution has an acid reaction; it forms crystalline, sweet salts with alkaloids and metallic bases. Solutions of alkalis and their carbonates dissolve it, forming compounds.

**Soluble** 1 in 400 of water, 1 in 38 of alcohol 90%, 1 in 100 of ether, and about .1 in 50 of glycerin, slightly soluble in chloroform, oils, fats and acetone.

**Use.** Instead of sugar for diabetic and obese patients.

Saccharin (insoluble) is sold in sweetening powers 300, 450 and 550—the above remarks refer to “550.”

**Elixir Saccharini** (B.P.C.). **Syn.** ELIXIR GLUSIDI.

**Dose.**—5 to 20 minims (0.3 to 1.2 ml.).

Saccharin 1 in 20 dissolved with sodium bicarbonate in alcohol and water. 1% added to mixtures for flavouring.

**Tabellæ Saccharini** (B.P.C.) contain  $\frac{1}{2}$  gr. (0.02 g.) of soluble saccharin.

**Saccharinum Solubile** (B.P., U.S.P. XI, P.G. VI, P. Helv. V, P. Dan.).  $\text{CO} \cdot \text{C}_6\text{H}_4 \cdot \text{SO}_2\text{NNa} \cdot 2\text{H}_2\text{O} = 241.1$  **Syn.** GLUSIDUM SOLUBILE.

**Dose.**— $\frac{1}{2}$  to 2 grains (0.03 to 0.12 g.).

The sodium derivative of saccharin, of which it contains about 90%. Occurs as a white crystalline or granular powder.

**Soluble** 1 in  $1\frac{1}{2}$  of water at 25°, 1 in 50 of alcohol 90% at 25°. As a sweetening agent, 1 in 2000 or 2 gr. to an 8-oz. mixture is sufficient.

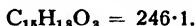
**Dulcin.**  $\text{C}_9\text{H}_7\text{OC}_6\text{H}_4\text{NHCONH}_2 = 180.1$  **Syn.** *p*-PHENETOI CARBAMIDE (P.G. VI)

**Dose.**—Tablets are made containing  $\frac{1}{2}$  grain (0.05 g.).

White crystalline powder, m.p. 172° to 174°. Slightly soluble in water, readily in alcohol. Used as a substitute for sugar, and stated to be innocuous.

## SANTONINUM

(with ARECA and CHENOPODIUM, etc.)

B.P., U.S.P. XI, P. *Helv.* V, P. *Dan.*, F.E. VIII.

**Dose.**—1 to 3 grains (0.06 to 0.2 g.). U.S.P. XI average dose 1 grain. *Fr. Cx.* has max. single dose  $1\frac{1}{2}$  grains, max. during 24 hours 5 grains approx. Owing to the possibility of idiosyncrasy, the first dose should not exceed 1 grain for a child, or 3 grains for an adult.

A neutral crystalline principle. The inner anhydride, or lactone, of santonic acid, obtained from *santonica*. M.p.  $171^{\circ}$  to  $174^{\circ}$ . Should be protected from light, otherwise it turns yellow (*see* Golden Santonin).

**Soluble** 1 in 50 of alcohol 90%, 1 in 3 of boiling alcohol 90%, 1 in  $2\frac{1}{2}$  of chloroform, 1 in 140 of ether, 1 in 200 of castor oil; also soluble in other oils and in caustic soda solution. Insoluble in water.

**Antidotes.** Empty stomach by emetic or stomach tube. Give purgative dose of calomel. Demulcent drinks, but *not* oils or fats. Chloral hydrate by rectum for convulsions. Stimulants. Artificial respiration if necessary.

In children, 0.06 g. has produced serious poisoning, and two such doses have been fatal.—*J. Amer. med. Ass.*, 11/1935, 1212

**Uses.** It is an anthelmintic for round-worms (*Lumbrici*) and thread-worms (*Ascarides*), but is inoperative against tape-worm (*Tænia*). It colours the urine orange if acid, or purplish red if alkaline, and in too large a dose may cause objects to appear of a green or yellow colour. The usual custom is to give the santonin in powder on 2 or 3 nights, following by castor oil or a saline purge in the morning. The flow of bile is particularly useful in making the worm let go its hold. Given in powder, the drug is not absorbed and is non-toxic. It is often given with calomel or compound powder of scammony, the subsequent administration of a purge then being unnecessary. It is very active in oily solution and is sometimes prescribed with castor oil, the santonin being dissolved in the oil and the solution emulsified with acacia. Poisoning has, however, occurred from administration in oily solution.

**Confectio Santonini Composita** (P.E.H.C.). Santonin 1 gr., ginger 1 gr., jalap 3 gr., sulphur 4 gr., confection of senna 51 gr. For a child 2 to 5 years.

**Suppositorium Santonini** contains 3 gr. (0.2 g.) or more. Should be inserted every second or third night, for three times.

**Tabellæ Santonini** (B.P.C.) contain 1 gr. (0.06 g.), in chocolate basis.

**Tabellæ Santonini et Hydrargyri Subchloridi** (B.P.C.)  
*Syn.* TABELLÆ SANTONINI COMPOSITÆ.

**Dose.**—1 or 2 tablets.

Contain santonin 1 gr. and mercurous chloride 1 gr.



**Tabellæ Santonini et Scammoniae Compositæ (B.P.C.)****Dose.**—1 tablet.

Contain santonin  $1\frac{1}{2}$  gr., compound powder of scammony 2 gr., and mercurous chloride  $\frac{1}{2}$  gr. **Pulvis Santonini Compositus** (*Gt. Orm. H.*) has the same composition. A saline should be given next morning.

**Trochisci Santonini (B.P.C.)** contain 1 gr.**Golden Santonin.** *Syn.* CHROMO-SANTONIN.**Dose.**—2 to 5 grains (0.12 to 0.3 g.).

A modification of ordinary santonin formed by exposure to sunlight.

ENTERIC is stated to have been usefully treated, also a type of 'sprue' (3-grain doses morning and evening in oil), and dysentery.

**Sodii Santoninas**,  $\text{NaC}_{11}\text{H}_{13}\text{O}_4 \cdot 3\frac{1}{2}\text{H}_2\text{O} = 349.2$ .**Dose.**— $\frac{1}{2}$  to 1 grain (0.016 to 0.06 g.) for adults. White crystals. Should in preference be given in salol-coated pills or tablets.Has been used as anthelmintic.—T. A. Henry, *Pharm. J.*, 1/1923, 28.**Santonica (B.P.C.).** *Syn.* SEMEN CONTRA (*P. Helv. V*), SEMEN CINÆ, WORMSEED, FLORES CINÆ (*P.G. VI, P. Dan.*).The dried unexpanded flower heads of *Artemisia cina* (*Compositæ*). Contains 2 to 3.5% of santonin. Has been administered as a decoction or infusion for round-worms and thread-worms.Santonin from Scottish-grown *Artemisia maritima*; 0.81% found.—J. Coutts, *Pharm. J.*, 11/1929, 603.The examination of true and false santonicas.—T. E. Wallis and E. J. Mowat, *Pharm. J.*, 11/1925, 149.Two new crystalline principles isolated from Indian species of *Artemisia*—*Pharm. J.*, 1/1935, 3.**Absinthium (B.P.C., P. Helv. V, P. Dan.)** *Syn.* WORMWOODThe dried leaves and tops of *Artemisia Absinthium* (*Compositæ*). The active ingredient is the oil (0.3%). It is used as a tonic and digestive. Infusion 1 in 20.**Dose.**—1 to 2 ounces. The oil is contained in the drink absinthe. Other essential oils, e.g., anise, coriander, fennel, peppermint, hyssop, angelica and melissa are stated to be additional constituents.Absinthe-drinking in England. Absinthe should be prohibited in England, Vermouth and Chartreuse contain the oil of wormwood.—C. W. J. Brasher, *Lancet*, 1/1930, 844.**Tinctura Absinthii (B.P.C.).****Dose.**—1 to 4 drachms (4 to 16 ml.) 1 in 10.**Areca (B.P.C.).** *Syn.* SEMEN ARECÆ (*P.G. VI, P. Helv. V*), BETEL NUT.**Dose.**— $\frac{1}{2}$  to 1 drachm (1 to 4 g.).The dried ripe seeds of *Areca Catechu* (*Palmaceæ*).Is astringent, and is used as a vermifuge for tape-worm, especially for dogs, in doses of 2 gr. per lb. body weight. It is also used as a masticatory and added to dentifrices. Contains several alkaloids, the most active being the liquid alkaloid arecoline (about 0.1%),  $\text{C}_8\text{H}_{13}\text{NO}_2 = 155.1$ .**Arecolinæ Hydrobromidum (P.G. VI, Fr. Cx, P. Helv. V, P. Hung., P. Svec. X, P. Bor. VII, F.E. VIII).** $\text{C}_8\text{H}_{13}\text{O}_2\text{N} \cdot \text{HBr} = 236.0$ .**Dose.**—*P. Helv. V* gives max. single dose  $\frac{1}{10}$  gr., max. in 24 hours  $\frac{1}{10}$  grain approx.

White needles soluble in water. Physiological action is allied to that of pelletierine and pilocarpine. Is sialagogue and diaphoretic. A 1% solution has been used as a miotic but action is of

short duration Is given hypodermically as a cathartic in veterinary medicine, the dose for horses being about 1 grain; also given orally in doses of  $\frac{1}{16}$  to  $\frac{1}{2}$  grain as a tænicide for dogs

**BETEL NUT CHEWING.** The ingredients are betel leaf, areca nut, black catechu, lime, turmeric, paste and tobacco leaf. Details as to betel nut (oral) carcinoma In Siam betel nut chewing is more done by women than men The habit prevents decay of teeth, but leads to chronic changes of mucous membrane of the mouth, causing loosening and loss of teeth.—A. G. Ellis, *Brit. med. J.*, 11/1921, 808, *J. trop. Med. (Hyg.)*, 1922, 149.

**Buteæ Semen (B.P.C.).**

*Dose.*—10 to 20 grains (0.6 to 1.2 g.)

The seeds of *Butea frondosa* (Leguminosæ) Contains moodooga oil Anthelmintic like santonin. Administered as **Pulvis Buteæ Seminum**, the integuments being removed by soaking in water, the seeds then being dried and powdered

**Chenopodium (B.P.C.).** *Syn.* AMERICAN WORMSEED.

*Dose.*— $\frac{1}{2}$  to 1 drachm (1 to 4 g.).

The fruit of *C. ambrosioides* var. *anthelminticum*. Contains 1% of volatile oil. Is a vermifuge for round-worms and hook-worms

**Oleum Chenopodii (B.P., U.S.P. XI, P. Helv. V).** *Syn.* OIL OF AMERICAN WORMSEED

*Dose*—3 to 15 minims (0.2 to 1 ml.). *U.S.P. XI* average dose 15 minims *P. Ned* has max. daily dose 22 minims. To be given at bedtime fasting, and followed by a purgative. Children of about 12 years of age may receive 20 m., washed out with salts 3 hours afterwards.

The oil distilled with steam from the fresh flowering and fruiting plants of *Chenopodium ambrosioides* var. *anthelminticum*. Contains not less than 65% w/w of ascaridole,  $C_{10}H_{16}O_2$ . *U.S.P. XI* requires 60 to 80% of an acetic acid soluble fraction.

Anthelmintic for hook-worms and round-worms. The worms are paralysed by the oil and must be expelled by a purge.

**ANKYLOSTOMIASIS** **Uncinariasis** **Commission of the Orient** The oil in small doses is more efficient than similar dose of thymol—*Lancet*, 1/1921, 235.

The maximum individual dose for hookworm appears to be 1 ml., but three capsules, each containing 0.5 ml., may be given at 2-hourly intervals, followed 3 hours later by 1 oz. of magnesium sulphate—*Lancet*, 1/1922, 1057

Oil is preferable to thymol, though the after-effects—giddiness, deafness, burning in stomach and headache—are more pronounced—Rockefeller Foundation Report, *Trop. Dis. Bull.*, 1921, 117

Signs of collapse after chenopodium treated with 1½ ml. Pituatrin intramuscularly.—D. C. Richards, per *J. trop. Med. (Hyg.)*, 1923, 69

Dangers of chenopodium oil Many cases of poisoning recorded—some fatal No other drug should be given with the anthelmintic.—*Brit. med. J. Epit.*, 1/1924, 57.

20,000 worm cases treated by a fresh mixture of 1 part with 7 of carbon tetrachloride—*J. trop. Med. (Hyg.)*, 1924, 31.

The secret of its correct use is to prevent absorption. Give in one sufficiently large dose and expel from the intestines by aperients.—*Brit. med. J. Epit.*, 11/1924, 86

Fatality after taking 10 g. within a week.—Per *J. Amer. med. Ass.*, 1/1926, 1175.

Brings away *A. lumbricoides*. One dose not always sufficient. A child of 3 received 2 m., finally working up to 10 m.—T. W. S. Paterson, July 24, 1928.

Oil of chenopodium has no stability. When in greatest vogue its active principle, ascaridole, was still undetermined This is deadly to man and worm, the respective lethal doses lie near one another, and its reported percentage in the oil has varied from 33 to 98. Further, the size of drops varies with

different droppers, and there has been catastrophic confusion between 45 drops on the International Dropper (or 2.2 ml.) and 45 minims (or 3 ml.). Numerous deaths have followed the latter, apparently none the former, which at a percentage of 66 implies 0.8 ml. of ascaridole. To give the oil without knowledge of its ascaridole content is indefensible—but customary. Many tens of thousands of doses have been reported, in few has its ascaridole content been known, and in none of these has deworming been the method of measurement. In other words, I find no acceptable published evidence of its efficiency against hookworms.—C. Lane, *Lancet*, 1/1935, 1461.

**Ascaridole** (*Burroughs Wellcome, London*). The separated active principle of the oil is also obtainable. *Dose*.—Adults, 12 to 20 minims (max 30 minims) To be given in three portions at intervals of 1 hour. Children  $\frac{1}{2}$  to  $\frac{3}{4}$  minims for a child of 2 years, increasing by  $\frac{1}{4}$  minim for every year of age up to 12, then by 1 minim per year up to adult age. May be administered on sugar or in any suitable vehicle. Castor oil or magnesium sulphate should be given after the last dose.

**Cucurbita** (*B.P.C., P. Helv. V*). *Syn.* CUCURBITÆ SEMINA PRÆPARATA, MELON PUMPKIN SEEDS.

*Dose*.—3 to 4 ounces, bruised with water or milk. The fresh ripe seeds of *C. maxima* (Cucurbitaceæ), deprived of testa and tegmen, and not more than a month old. Anthelmintic; give first a saline purge and afterwards castor oil

**Cusso** (*B.P.C.*) *Syn.* KOUSSO.

*Dose*.— $\frac{1}{2}$  to  $\frac{3}{4}$  ounce (8 to 16 g.) made into an infusion.

The dried panicles of fertilised pistillate flowers of *Brayera anthelmintica* (Rosaceæ). Contains the yellow amorphous body, kosotoxin. Anthelmintic, especially for tape-worm. Administered as an infusion (1 in 16), the dose being preceded by the administration thrice daily of 1 drachm doses of sodium bicarbonate, and by a saline purge, being taken on an empty stomach.

**Embelia** (*B.P.C.*).

*Dose*.—1 to 4 drachms (4 to 16 g.) Dried fruit of *E. ribes* and *E. robusta* (Myrsinaceæ). Anthelmintic, especially for tape-worm.

**Pepo**. Ripe seed of *Cucurbita Pepo* (Cucurbitaceæ), pumpkin. *Average dose*.—1 ounce. Said to be a good remedy for tape-worm, given before breakfast, followed by coffee and later a brisk cathartic.

## SAPONES

**Sapo Animalis** (*B.P.*), *syn.* CURD SOAP, consists mainly of sodium stearate. Sparingly soluble in cold water, completely soluble in hot water, almost completely soluble in alcohol 90%.

**Emplastrum Saponis Fuscum** (*B.P.C.*). *Syn.* EMPLASTRUM CERATI SAPONIS.

Prepared with curd soap, yellow beeswax, olive oil, lead monoxide and vinegar.

**Linimentum Saponis Camphoratum** (*B.P.C.*) *Syn.* SOLID OPODELDOC.

A solid liniment containing curd soap, camphor, oils of thyme and rosemary, dilute solution of ammonia and alcohol.

**Sapo Durus** (*B.P., U.S.P. XI*), *syn.* CASTILE SOAP, is made by saponifying olive oil with sodium hydroxide, and consists mainly of sodium oleate.

**Soluble** 1 in 20 of cold water, 1 in  $1\frac{1}{2}$  of hot water, almost completely soluble in cold alcohol 90%, completely soluble 1 in 2 of boiling alcohol 90%.

[P1 81] **Emplastrum Saponis** (*B.P.C.*) *Syn.* PLASTER OF SOAP

Hard soap about 1 in 7, with plaster of lead and colophony.

[D-P1 81] **Pilulæ Saponis cum Opio** (*B.P.C.*). *Syn.* PILULÆ SAPONIS COMPOSITÆ; COMPOUND SOAP PILLS.

Each pill contains  $\frac{1}{2}$  gr. of powdered opium and about 1 gr. of hard soap.

*Dose*.—1 or 2 pills.

**Sapo Superadipatus** (*P. Ned. V.*)

Wool fat 4, potash soap 16, hard soap 80

**Sapo Superadipatus cum Pice Liquida** (*P. Ned. V.*)

Wool fat 4, liquid tar 5, potash soap 11, hard soap 80.

**Sapo Superadipatus cum Sulfure Precipitato** (*P. Ned. V.*)

Wool fat 4, precipitated sulphur 10, potash soap 16, hard soap 70

**Sapo Kalinus** (*B.P.C., P.G. VI, P. Helv. V, P. Austr.*), *syn.*

**LINSEED OIL SOAP**, is made with linseed oil and potassium hydroxide. Soluble about 1 in 4 of water and 1 in 1 of alcohol 90%. **Sapo Mollis** (*U.S.P. XI*) is also made from linseed oil.

**Sapo Amygdalinus** (*F.E. VIII*) is made from almond oil and sodium hydroxide.

**Spiritus Saponis Kalini** (*B.P.C.*) *Syn* SPIRITUS SAPONIS KALINI (*HEBRA*)

An alcoholic solution of potash soap, perfumed with oil of lavender *P.G. VI* is 1 in 1 w/v in alcohol 90%

**Spiritus Saponatus** (*P.G. VI*)

Saponify olive oil 6 with solution of potassium hydroxide (15%) 7, and alcohol 7½ by agitation until it mixes clear with alcohol and water. Add then alcohol 22½ and water 17, filter

**Soap and Spirit Lotion.** Soft soap 1 in alcohol 90% q s to 2

**Sapo Mollis** (*B.P.*), *syn.* SAPO VIRIDIS, is made by saponifying olive oil (*U.S.P. XI*, linseed oil) with potassium hydroxide, and consists mainly of potassium oleate. Soluble 1 in 4 of water, 1 in 1 of boiling water and 1 in 1 of alcohol 90%

**Enema Saponis** (*B.P.C.*) *Dose*—20 ounces (600 ml) 5% w/v

**Linimentum Saponis** (*B.P.*) Soft soap 4, camphor 2, oil of rosemary 0.75, distilled water 8.5, alcohol 90% to 50.

**Linimentum Saponis Mollis** (*U.S.P. XI*) 65% of soft soap and 2% of oil of lavender in alcohol

**Liquor Saponis Æthereus** (*B.P.C.*) *Syn.* ETHER SOAP, SOLUTIO SAPONIS ÆTHERÆA

A solution containing about 40 to 50% of potassium oleate in alcohol and ether

[P1] **Liquor Saponis Antisepticus** (*B.P.C.*) is the same solution with the addition of 0.05% w/v of mercuric iodide and potassium iodide

**Pasta Mackintosh** (*R.V.I.*).

Soft soap 7, powdered pumice stone 7, prepared chalk 7, water 1, Cyllin 1

**Spiritus Saponatus** (*B.P.C.*) 65% w/v of soft soap in alcohol.

**Sapo Medicatus** (*P.G. VI, P. Dan, P. Helv. V*) is made from lard and olive oil and is chiefly sodium oleate

**Synol Soap** (*Johnson and Johnson, Slough*). A liquid soap containing 2½% of cresol.

The preparation of benzene and turpentine soaps, the latter having considerable bleaching power—*Pharm. J.*, 11/1927, 514

**Aluminium Soaps** are used in water-proofing textiles and in making certain plastic materials used as substitutes for rubber, leather and celluloid, also aluminium stearate as lubricating oil thickeners

**Ammonium Soaps** are employed in vanishing creams and other toilet preparations.

**Copper Soaps** are used for preserving fishing nets and in making anti-fouling paints for ships' bottoms, depending on the poisonous properties of copper salts

**Sodii Oleas.**  $\text{CH}_3(\text{CH}_2)_7\text{CH} : \text{CH}(\text{CH}_2)_7\cdot\text{COONa} = 304.3$ .

*Prop. Name.* EUNATROL (*Zimmer, Frankfurt; Coates & Cooper, London*).

*Dose.*—2 to 10 grains (0.12 to 0.6 g.).

Is given to dissolve gall-stones. Useful as cholagogue. Capsules of sodium oleate contain 5 gr.

CARCINOMA treated with sodium oleate by J. H. Webb (Melbourne) on Shaw-Mackenzie's theory that sodium oleate and various tissue extracts act as co-enzymes, i.e., activating the dormant *prolapse*. 20 grains of sodium oleate daily in pill form for a year and 30 injections of 10 ml of sodium oleate solution—beginning with  $\frac{1}{2}\%$  and increasing to 5%—Albert Wilson, *Fdinb med J*, May, 1925, 248

Oleic acid and sodium oleate were found on injection to modify the growth of tumours, confirming the clinical observations of Shaw-Mackenzie in 1913. The procedure might be useful to prevent regrowth after operation—*Lancet*, 1/1925, 1193

Subcutaneous injections of 1 to 3 ml of sodium oleate solution 0.8% have been found of benefit in cancer of the breast—J. Shaw Mackenzie, *J. trop Med (Hyg.)*, 1927, 85

**Sodii Stearas** (U.S.P. XI) is a mixture of the stearate ( $\text{NaC}_{18}\text{H}_{35}\text{O}_2$ ) and palmitate ( $\text{NaC}_{16}\text{H}_{31}\text{O}_2$ ). A white powder soapy to the touch. Slowly soluble in cold water or alcohol, readily in hot.

### **Saponinum** (B.P.C.) *Syn* QUILLAIC ACID, QUILLAIN

A colloidal glycoside or mixture of glycosides obtained from quillaja bark. An intensely irritating and sternutatory powder. Aqueous solutions froth readily when shaken. Has hæmolytic action on blood. Is used as an emulsifying agent for oils in external applications and as a foam stabiliser in contraceptive tablets.

Death from saponins is preceded by a long incubation period with the symptoms of central paralysis. Fish die when the water they are in contains 1 in 100,000. Saponin in salt and carbolic acid baths is said to aid the action of all drugs which stimulate the skin. The nasal mucous membrane is stimulated and produces copious skin secretions by the action of dilute spray, gargle or irrigation. Saponins are anthelmintic and diuretic.

Saponins, various, described—J. G. Driver and A. G. Trease, *Pharm J*, 1/1927, 623

Usual views as to hæmolytic action of saponins when taken orally are contradicted. A man can take as a single daily dose as much as 4 g. without any damage resulting, since it does not pass through the intestinal walls and is decomposed by digestive enzymes. Administration facilitates absorption of Ca and Mg. Nutritive value of spinach may be due to saponin content just as much as to its content of iron, chlorophyll or vitamins—L. Kofler, *Apothekerztg*, 1933, 702

### **Triethanolamina** (B.P.C.).

A colourless, almost odourless, syrupy liquid with strongly alkaline reaction. Consists chiefly of trihydroxytriethylamine,  $(\text{CH}_2\text{CH}_2\text{OH})_3\text{N}$ , with small proportions of the di- and mono-hydroxy compounds. Forms crystalline salts with mineral acids, the hydrochloride has m.p.  $173^\circ$  to  $174^\circ$ .

**Miscible** with water and alcohol 90%; slightly soluble in ether.

Is a useful emulsifying agent for preparations for external use when used in conjunction with oleic or stearic acid, with which the corresponding salts are formed.

**Quillaia** (B.P., P. Hek. V, P. Dan.) *Syn* PANAMA BARK, SOAP BARK.

**Dose.**—1 to 3 grains (0.06 to 0.2 g.).

The dried inner part of the bark of *Quillaja Saponaria* and other species (Rosaceæ). Contains quillaic acid,  $\text{C}_{19}\text{H}_{30}\text{O}_{10} = 418.3$ ,

and sapotoxin,  $C_{17}H_{28}O_{10} = 408.2$ , closely allied to saponin. Has a sweetish but acid after-taste and possesses emulsifying properties, causing frothing in water in which it has been macerated. Its lather kills pediculi of scalp. Soap bark has been used as an expectorant in bronchitis, is contraindicated in inflammation of the intestines or stomach, or ulcerated condition of the mucous membrane. Is used as an emulsifier.

**Extractum Quillaiae Liquidum (B.P.C.)** 1 in 1

**Tinctura Quillaiae (B.P.)**

1 in 20 of alcohol 45%. Five minims of this will emulsify 1 drachm of fixed oil

## SCILLA

*B.P., P. Helv. V, P. Dan*

**Dose.**—1 to 3 grains (0.06 to 0.2 g.).

The bulb of *Urginea Scilla* (Liliaceae) (*U. maritima* U.S.P. XI) with membranous outer scales removed, cut into slices and dried. Resembles digitalis in action. It is also expectorant and more diuretic.

Squill preparations of the U.S.P. XI are biologically standardised.

**Antidotes.** Treat as for poisoning by digitalis, see p. 441.

**Acetum Scillae (B.P., U.S.P. XI)**

**Dose.**—10 to 30 minims (0.6 to 2 ml.).

Squill 10% w/v macerated in dilute acetic acid

**Extractum Scillae Liquidum (B.P.C.).**

**Dose**—1 to 3 minims (0.06 to 0.2 ml.). 1 in 1.

**FOR RATS.** Liquid extract of red squill is efficacious. Add to bread and milk. Comparatively harmless to larger animals, advocated by Min. of Agriculture—*Pharm. J.*, ii/1927, 524.

The rat-poisoning substances appear to be present in significant amounts in the red squills only—F. R. Winton, *J. Pharmacol.*, June, 1927, 137.

**Linctus Scillae (B.P.C.)** *Syn.* LINCTUS, SIMPLE LINCTUS.

**Dose**— $\frac{1}{2}$  to 1 drachm (2 to 4 ml.).

Oxymel of squill 1 in 4 with mucilage of tragacanth, glycerin, emulsion of chloroform and syrup.

**Mist. Oxymellis (N.I.F.)** Oxymel of squill 30 m., liquid extract of ipecacuanha  $\frac{1}{2}$  m., glycerin 20 m., dilute sulphuric acid 4 m., solution of bordeaux B 2  $\frac{1}{2}$  m., water to  $\frac{1}{2}$  oz.

[P1] **Mist. Scillae Co. (N.I.F.).** Oxymel of squill 30 m., camphorated tincture of opium 15 m., tincture of ipecacuanha 10 m., water to  $\frac{1}{2}$  oz.

**Oxymel Scillae (B.P.).**

**Dose.**— $\frac{1}{2}$  to 1 drachm (2 to 4 ml.).

Contains equivalent of 5% w/v of squill in acetic acid, honey, and distilled water.

**Pilulæ Scillæ Compositæ (B.P.C.).***Dose.*—1 or 2 pills.

Contain squill 1 gr., ginger  $\frac{1}{2}$  gr., ammoniacum  $\frac{1}{2}$  gr., and hard soap about  $\frac{1}{2}$  gr.

**Syrupus Scillæ (B.P.).***Dose.*— $\frac{1}{2}$  to 1 drachm (2 to 4 ml.).

Contains 45% *v/v* of vinegar of squill.

**Syrupus Scillæ (U.S.P. XI).** *Average dose*—30 minims (2 ml.)

Vinegar of squill 45, sucrose 80 in water to 100

**Tinctura Scillæ (B.P.).***Dose.*—5 to 30 minims (0.3 to 2 ml.).

Contains equivalent of 10% *w/v* of squill.

**Tinctura Scillæ (U.S.P. XI)** *Average dose*—15 minims (1 ml.)

Strength 1 in 10.

**Scillaren** (*Sandoz, London, Brooks & Warburton, London*) Preparations of the total glycosides of squill *Dose*—2 tablets (ea 0.0008 g.) or 40 drops of solution (0.0008 g. per ml.) 3 or 4 times daily, in urgent cases intravenously not more than 1 ampoule (1 ml. = 0.0005 g.) per day Valvular lesions, œdema of cardiac origin, chronic myocarditis and "weak heart"

**Urginea (B.P.C.).** *Syn.* INDIAN SQUILL The sliced younger bulbs of *U. indica* (Liliacæ) Is used in the East in place of squill, and preparations of *urginea* are made and used in the same way as those of squill

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**SENEGA**

*B.P., P. Helv. V, P. Dan., P. Belg. IV*

*Dose.*—6 to 12 grains (0.4 to 0.8 g.).

The dried root of *Polygala Senega* (Polygalacæ). An expectorant; contains senegin.

**Extractum Senegæ Liquidum (B.P.)***Dose*—5 to 15 minims (0.3 to 1 ml.).

1 in 1 of alcohol 60%, rendered faintly alkaline with ammonia  
Litmus is a suitable indicator.

**Infusum Senegæ Concentratum (B.P.).***Dose.*— $\frac{1}{2}$  to 1 drachm (2 to 3 ml.).

1 in 2 $\frac{1}{2}$  of alcohol 25%, rendered faintly alkaline with ammonia.

**Infusum Senegæ Recens (B.P.)***Dose.*— $\frac{1}{2}$  to 1 ounce (15 to 30 ml.). 1 in 20.

**Tisane de Polygala (Fr. Cx.)**, 1 in 100 of boiling water, infuse  $\frac{1}{2}$  hour

**Mist. Seneg. Ammon. (N.I.F.).** *Syn.* MIST IPECAC. CO

Ammonium carbonate 3 gr., tincture of ipecacuanha 5 m., liquid extract of squill 2 m., liquid extract of senega 6 m., water to  $\frac{1}{2}$  oz

**Tinctura Senegæ (B.P.).***Dose.*— $\frac{1}{2}$  to 1 drachm (2 to 4 ml.).

Liquid extract of senega 1 in 5, with alcohol 60%.

**Cocillana.** *Dose.*—8 to 15 grains (0.5 to 1 g.).

The bark of a South American plant, *Guarea Rusbyi* (Meliacæ), stated to equal ipecacuanha in expectorant properties and to be, in addition, tonic and laxative.

[P1] **Cocillana Compound Syrup** (*Parke, Davis, London*). Expectorant combination, containing per oz.: tincture of cocillana 40 m., tincture of euphorbia 120 m., syrup of wild lettuce 120 m., fluid extract of squill 2 m., fluid extract of senega 2 m., potassium antimonytartrate  $\frac{1}{4}$  gr., cascarn 8 gr., ethylmorphine hydrochloride  $\frac{1}{4}$  gr., menthol  $\frac{1}{100}$  gr. Dose— $\frac{1}{4}$  to 1 drachm 3 or 4 times daily.

[P1 81] **Prunus Serotina** (*B.P., U.S.P. XI*). *Syn.* PRUNI VIRGINIANÆ CORTEX, WILD CHERRY BARK.

Dose.—15 to 30 grains (1 to 2 g.).

The bark of *Prunus serotina* (*Rosaceæ*) Contains prunasin and a cyanogenetic enzyme, and may yield from 0.075 to 0.16% of HCN. Used for relief of cough in phthisis, etc.

[P1] **Syrupus Pruni Serotinæ** (*B.P.*) *Syn.* SYRUPUS PRUNI VIRGINIANÆ, SYRUP OF WILD CHERRY.

Dose.— $\frac{1}{2}$  to 2 drachms (2 to 8 ml.).

A solution of sucrose in an aqueous glycerin percolate, containing the equivalent of 15% *w/v* of the bark

[P1] **Syrupus Pruni Virginianæ** (*U.S.P. XI*) Average dose—2 $\frac{1}{2}$  drachms Wild cherry bark 15, sucrose 80, glycerin 5, alcohol 2, water to 100

[P1] **Tinctura Pruni Serotinæ** (*B.P.C.*) *Syn.* TINCTURA PRUNI VIRGINIANÆ.

Dose— $\frac{1}{2}$  to 1 drachm (2 to 4 ml.) 1 in 5

**Stillingia** (*B.P.C.*) *Syn.* QUEEN'S ROOT, YAW ROOT

Dose— $\frac{1}{2}$  to  $\frac{1}{4}$  drachm (1 to 2 g.)

The dried root of *Stillingia sylvatica* (*Euphorbiaceæ*) Contains volatile oil. Large doses emetic, cathartic, small doses alterative Is employed in scrofula, syphilis, jaundice, and for piles

## SENNÆ

**Sennæ Folium** (*B.P.*). *Syn.* SENNA (*U.S.P. XI*).

Dose—10 to 30 grains (0.6 to 2 g.).

The dried leaflets of *Cassia acutifolia* (*Alexandrian*) or *C. angustifolia* (*East Indian or Tinnevely*) (*Leguminosæ*). *P. Helv. V* and *P. Dan* recognise *C. angustifolia* only. Contains aloemodin, kempferol, isorhamnetin, etc. Senna acts only on the colon, causing peristalsis. It has little or no action on peristalsis of the stomach and small intestine.

**Confectio Sennæ** (*B.P.*). *Syn.* LENITIVE ELECTUARY.

Dose.—1 to 2 drachms (4 to 8 g.).

Contains senna 10% with coriander, figs, tamarind, cassia, prunes, extract of liquorice, sugar and water. The use of coriander oil instead of the fruit has been suggested.

**Confectio Sennæ Composita** (*C.X.H.*). Powdered jalap 3 gr., senna leaf 3 gr., sublimed sulphur 3 gr., black treacle to 60 gr

**Confectio Sennæ et Sulphuris** (*B.P.C.*).

Dose.—1 to 2 drachms (4 to 8 g.).

Equal parts of confection of senna and confection of sulphur.

**Fluidextractum Sennæ** (*U.S.P. XI*). Average dose.—30 minims (2 ml.). 1 ml. represents 1 g. of senna leaf.

**Syrupus Sennæ** (*U.S.P. XI*). Average dose.—2 drachms (8 ml.).

Fluidextract of senna 25, oil of coriander 0.5, sucrose 63.5 in water to 100.



**Tinctura Sennæ Composita (B.P. ('))**

*Dose.*— $\frac{1}{4}$  to 1 drachm (2 to 4 ml.) for repeated administration, 2 to 4 drachms (8 to 16 ml.) for a single administration.  
Senna leaf 1 in 5, with caraway and coriander.

**Sennæ Fructus (B.P., P. Helv. V) Syn. SENNA POD**

*Dose*—10 to 30 grains (0.6 to 2 g.); corresponding to about 4 to 12 pods.

The dried ripe fruits of either Alexandrian or Tinnevely senna. *P. Dan.* recognises *C. angustifolia* only. These are stronger than the leaves.—Tschirch. The legumes are more active if green.

**Elixir Sennæ (B.P.C.). Syn. LIQUOR SENNÆ LEGUMINORUM DULCIS**

*Dose.*— $\frac{1}{2}$  to 1 drachm (2 to 4 ml.).

A flavoured preparation containing 50% *v/v* of liquid extract of senna.

**Extractum Sennæ Liquidum (B.P.)**

*Dose*—10 to 30 minims (0.6 to 2 ml.).

1 in 1, by maceration in chloroform water, evaporation, and addition of alcohol.

**Infusum Sennæ Concentratum (B.P.)**

*Dose.*— $\frac{1}{2}$  to 2 drachms (2 to 8 ml.).

1 in  $1\frac{1}{2}$  by percolation with alcohol 20% and addition of 1 in  $12\frac{1}{2}$  of strong tincture of ginger.

**Infusum Sennæ Recens (B.P.).**

*Dose.*— $\frac{1}{2}$  to 2 ounces (15 to 60 ml.).

Senna 1 in 10 and ginger 1 in 200

**Mistura Sennæ Composita (B.P.) Syn. BLACK DRAUGHT**

*Dose.*—1 to 2 ounces (30 to 60 ml.).

Magnesium sulphate 1 in 4 with liquid extract of liquorice, compound tincture of cardamom, aromatic spirit of ammonia and infusion of senna.

**Syrupus Sennæ (B.P.).**

*Dose.*— $\frac{1}{2}$  to 2 drachms (2 to 8 ml.).

Liquid extract of senna 25% *v/v* with oil of coriander, sucrose and water.

**Lixen** (*Allen & Hanburys, London*). Elixir of senna pods 1 drachm 10 large senna pods. Also in lozenges and pastilles.

**Baptisia (B.P.C.) Syn. WILD INDIGO ROOT.**

The dried root of *B. tinctoria* (Leguminosæ) Has laxative properties and has been given as a decoction

**Tinctura Baptisæ (B.P.C.)** 1 in 10. Occasionally added to mouth-washes for its saponin content.

**Baptisin.** *Dose.*—1 to 5 grains An extractive from baptisia, in small doses laxative, in large doses cathartic. The mother tincture of baptisia (homœopathic) has a reputation for treatment of boils.

**Ficus** (*B.P.C.*). *Syn.* FIG, *CARICA* (*P. Helv. V*)

The dried fruit of *F. Carica* (*Moraceæ*), a mild laxative.

**Syrupus Ficorum** (*B.P.C.*).

*Dose.*— $\frac{1}{2}$  to 2 drachms (2 to 8 ml.).

Is prepared by dissolving sucrose in an aqueous decoction.

**Syrupus Ficorum Compositus** (*B.P.C.*) *Syn.* SYRUPUS FICORUM AROMATICUS.

*Dose.*— $\frac{1}{2}$  to 2 drachms (2 to 8 ml.).

Contains compound tincture of rhubarb, liquid extract of senna, elixir of cascara sagrada and syrup of figs.

**Ficin.** The sap of the fig tree, used by the natives of S. America for the treatment of intestinal parasites, has recently been investigated as an anthelmintic, and has been found to remove about 80% of *Trichuris*, as compared with the 20 or 25% removed by most other substances and the 40 or 50% removed by hexyl-resorcinol. The active principle is a proteolytic enzyme which digests the parasites. It is non-irritating and non-toxic if no lesion of the intestinal tract is present, in which case it causes dangerous erosion of the mucous membrane.—P. D. Lamson and co-workers, *J. Amer. med. Ass.*, 11/1932, 293.

**Morus** (*B.P.C.*). *SYN.* MULBERRY

The fresh ripe fruit of *M. nigra* (*Moraceæ*.)

**Syrupus Mori** (*B.P.C.*).

*Dose.*— $\frac{1}{2}$  to 1 drachm (2 to 4 ml.).

A solution of sucrose in mulberry juice

**Prunus** (*B.P.C.*). Prune is the dried ripe fruit of *P. domestica* var. *Juliana* (*Rosaceæ*). Has laxative properties

**Cerasus.** Red cherry is the fruit of *Prunus Cerasus* var. *capromana*.

**Syrupus Cerasi** (*B.P.C.*)

*Dose.*— $\frac{1}{2}$  to 1 drachm (2 to 4 ml.)

A solution of sucrose in red cherry juice. A flavouring and colouring agent

**Prunol** (*Prunol Products, London*). Prune jelly containing prunes, green ginger and about 7½% of senna. For constipation and colitis—action continues several days. Clears the colon of matter and relieves toxæmia

**Ribes Nigrum.** The fresh ripe fruit of the black currant.

**Syrupus Ribis Nigri** (*B.P.C.*)

*Dose.*— $\frac{1}{2}$  to 1 drachm (2 to 4 ml.). A solution of sucrose in the juice expressed from a mixture of black currants and red cherries.

**Ribes Rubrum.** The fresh ripe fruit of the red currant.

**Syrupus Ribis Rubri** (*B.P.C.*)

*Dose.*— $\frac{1}{2}$  to 1 drachm (2 to 4 ml.). A solution of sucrose in the juice expressed from a mixture of red currants and red cherries.

**Tamarindus** (*B.P.*).

The fruits of *Tamarindus indica* (*Leguminosæ*) freed from the brittle outer part of the pericarp and preserved with sugar. Occurs as a reddish-brown moist sugary mass. Contains tartaric acid, potassium acid tartrate and about 30% of sugar. Is also imported pressed into a solid mass as pulp (*Pulpa Tamarindi cruda, P. Helv. V*).

**Pastilli Tamarindorum Compositi** (*P. Austr. Add. VIII*). Tamarind pulp 10, senna in fine powder 3, sugar 5, wheat starch 1. Mix on water bath. Divide into pastilles weighing about 40 grains each and cover with chocolate. Laxative for children and invalids.

**SINAPIS NIGRA***B.P.C.**Syn.* SEMEN SINAPIS (*P. Helv. V, P. Austr., F E VIII, P. Ital. V, P. Belg. IV*)

Black mustard is the dried ripe seeds of *Brassica nigra* (*Cruciferae*). *U.S.P. XI* allows *B. nigra* also *B. juncea* and varieties of these species.

They contain the glycoside, sinigrin, and the enzyme, myrosin, which interact in the presence of water to yield allyl isothiocyanate (0.6 to 1%).

**Sinapis Alba** is obtained from *S. alba*. It yields no allyl isothiocyanate. **Bath Mustard** is powdered mustard from which the seed coats have not been completely removed. **Mustard Bran** consists usually of the seed coats of black mustard. **Mustard Flour** consists of powdered black and white seeds from which the seed coats have been largely removed.

**Uses.** As an emetic a tablespoonful in half a pint of warm water. In small doses is a stomachic and appetiser. Externally, a counter-irritant when applied as a poultice, or added to hot water and used as a foot-bath. It may blister tender skins.

**Balneum Sinapis** (*B.P.C.*). Contains 12 oz. of bath mustard per 30 gallons.

**Cataplasma Sinapis** (*B.P.C.*). Mustard flour 2% in linseed poultice.

**Emplastrum Sinapis** (*U.S.P. XI*). A spread plaster on paper, cloth or other material, prepared with oil-free black mustard and rubber solution, each sq. cm. contains at least 0.025 g. of the mustard. It should be applied after moistening with tepid water. **Charta Sinapisata** (*P. Helv. V*) contains 0.03% of  $C_3H_5NCS$ . Is also official in *P. Dan*.

**Oleum Sinapis Expressum** (*B.P.C.*) *Syn.* BLACK MUSTARD OIL.

Obtained by expression from black mustard seeds, the average content is about 26%. A brownish-yellow or greenish-brown oil used as a mild rubefacient. **White Mustard Seed Oil**, from the seeds of *B. alba*, is used for lubricating and for burning.

Comparison of Chinese colza oil (*ex Brassica campestris* var. *Chinoleifera*), black mustard, white mustard, rape oil and other varieties.—*Pharm. J.*, 1/1921, 519.

**Oleum Sinapis Volatile** (*B.P.C., U.S.P. XI, P. Helv. V*).

**Dose.**—No dose given in *B.P.C.* *U.S.P. XI* has average dose  $\frac{1}{2}$  minim.

Consists chiefly of allyl isothiocyanate,  $C_3H_5NCS$ , and may be prepared synthetically or distilled from black mustard seeds after expression of the fixed oil and maceration in tepid water to allow interaction between the glycoside, sinigrin (potassium myronate), and the enzyme, myrosin. *B.P.C.* requires not less than 92% of  $C_3H_5NCS$ .

**Linimentum Sinapis** (*B.P.C.*).

Volatile oil of mustard 3.5% in a castor oil, camphor and alcohol mixture.

**Spiritus Sinapis** (*P.G. VI*). Volatile oil of mustard 1, alcohol (90%) 49.

**Analgit** (*Analgit Co., Manchester; Braun, London*). Solution of allyl isothiocyanate with extracts of capsicum and arnica and 8% salicylates. A hyperæmic application for rheumatism, etc.

**Thiosinamina** (*B.P.C., F.E. VIII*).  $\text{CS}(\text{NH}_2)\text{NHC}_2\text{H}_5 = 116.1$ . *Syn.* RHODALLIN, ALLYLTHIOUREA, ALLYL-SULPHOCARBAMIDE.

**Dose** —Internally,  $\frac{1}{2}$  grain gradually increased to  $1\frac{1}{2}$  grains (0.03 to 0.1 g.) (with caution—in capsule or alcoholic solution). Hypodermically 1 to  $1\frac{1}{2}$  grains as *Injectio Thiosinaminæ et Sodii Salicylatis*

White crystals, usually with a slight garlic-like odour, and having a bitter taste. M.p.  $72^\circ$  to  $74^\circ$ . May be obtained by the interaction of volatile oil of mustard, alcohol and ammonia solution

**Manufacture.** To essential oil of mustard 456 g add in portions strong solution of ammonia 200 g. in alcohol 200 ml. The mixture becomes hot (or slight warming may be required to promote interaction)—cool down below  $40^\circ$ , and shake until the odour of the mustard oil disappears. Evaporate at  $40^\circ$  to about 650 g and leave to crystallise. Recrystallise from water. Evaporate mother liquor and wash further crop of crystals with water and then with ether.

**Soluble** 1 in 17 of water, about 1 in 2 of alcohol 90%, and in ether. Readily soluble in solutions of borax, urethane, benzoates, cinnamates, etc.

**Uses.** To some extent internally, but chiefly by injection (*vide infra*) with sodium salicylate, for absorbing fibrous and scar tissue. Has been used for keloid and in scleroderma. In ophthalmology it has been used in corneal opacity, corneal scars, choroiditis and other conditions.

TINNITUS AURIUM has been treated by 5% aqueous solution hypodermically with improvement, dose being increased from 6 to 35 m, also a 10% solution and a 20% glycerin solution. Should be tried before operating on the middle ear or labyrinth for this trouble

PERICARDIAL ADHESIONS have been treated by 3-gr doses in 80 m of water every other day in the flanks for 30 days

SCAR KELOID resulting from a burn received 5 injections of thiosinamine 0.2 g. with 1 day's interval between each. Produced poisoning symptoms, sweating headache (lasting 2 to 8 days). Ultimately the treatment was curative (after 18 injections).

Caution is needed whenever the patient experiences headache after the first injection of thiosinamine

### **Injectio Thiosinaminæ et Sodii Salicylatis (B.P.C.)**

**Dose** —8 to 15 minims (0.5 to 1 g.).

Contains 10% w/v of thiosinamine dissolved with aid of sodium salicylate in diluted glycerin

**Uses.** For relaxing scar tissue, in strictures of the gullet, urethra and rectum, in stenosis of the pylorus, rheumatoid arthritis, Dupuytren's contraction and eye affections (corneal infiltrations). Massage and stretching or the use of bougies in appropriate cases may be of value. Also in middle-ear disease and for tinnitus (but the "remote action" in such is doubtful), and in pleural adhesions, injected locally or into the gluteal muscles once or twice weekly according to severity of case. Has

been tried in lupus. It may be of value in arteriosclerosis, chronic rheumatism and paralysis.

**Cicatricine** (*Martindale, London*) Injection of thiosinamine and phenazone containing per ml. 3 gr. of thiosinamine, 5 gr. of phenazone and  $\frac{1}{10}$  gr. of benzamine lactate. A non-toxic, non-irritating injection for the treatment of cicatricial tissue.

**Compound Thiosinamin Sterules** (*Martindale, London*) contain 1 gr. of thiosinamine and  $1\frac{1}{2}$  gr. of sodium salicylate in 1 ml. of a special solvent.

**Fibrolysin** (*Merck, Darmstadt, Martindale, London*) Thiosinamine sodium salicylate. Supplied in ampoules (2.3 ml.), suppositories (0.3 g.) and lymph tubes (for the eye). *Dose*—1 ampoule intragluteally 2 to 3 times daily, 1 suppository at night, or 1 to 3 drops into the eye thrice daily.

### **Thiosinaminæ et Æthylis Iodidum.**

$\text{CS}(\text{NH}_2\text{C}_2\text{H}_5\text{I})\text{NHC}_3\text{H}_5 = 272.1$ . *Syn* TIODINE (*Cognet, Paris, Roberts, London*), THIODIN.

*Dose*.—1 to 4 grains (0.06 to 0.25 g.) daily by mouth; 3 to 6 grains (0.2 to 0.4 g.) three times weekly by injection.

Prepared by heating thiosinamine and ethyl iodide under a reflux condenser. Forms white crystals melting at about  $70^\circ$ .

**Soluble** 1 in 10 of water and 1 in 1 of alcohol 90%.

**Used** for the same purposes as thiosinamine, also given internally in intractable rheumatoid arthritis. Skin rashes may follow its oral administration.

**ACTINOMYCOSIS** 5 cases treated hypodermically with rapid and complete success.—T. G. Moorhead, *Brit med J.*, 1/1929, 419

**Iodolysin** (*Allen & Hanburys, London*) A similar preparation, stated to contain 43% thiosinamine and 47% of I **Iodolysin** solution for oral use, 30 m. containing 2 gr. Iodolysin; also **Injection** (hypodermic) 15 m. containing 2 gr. **Ointment and Pigment** are also prepared. To soften cicatrices and promote absorption of fibrous tissue. Of value in rheumatoid arthritis.

**RHEUMATOID ARTHRITIS** improved by Iodolysin internally.—*Brit med J.*, 11/1925, 1040.

**Armoracia** (*B.P.C.*) Horseradish is the fresh root of *Cochlearia Armoracia* (*Cruciferae*). Contains sinigrin (potassium myronate) and the enzyme myrosin, which react in the presence of water to give allyl isothiocyanate. The infusion, 1 in 20, has been given as a stimulant.

**Spiritus Amoriaci Compositus** (*B.P.C.*)

*Dose*.—1 to 2 drachms (2 to 4 ml.).

A distilled spirit representing 1 in 8 of horseradish. Administered as a carminative.

**Mezereum** (*B.P.C., P. Helv. V.*) *Syn.* MEZEREON.

*Dose*.—8 grains (0.5 g.). The dried bark of *Daphne Mezereum* (*Thymelæaceæ*), and other species. Contains an acrid resin and a bitter glycoside (daphnin). Formerly used as an epispastic and stimulant.

## **SODIUM**

$\text{Na} = 22.997$ .

### **Liquor Sodii Æthylatis** (*B.P.C.*).

A 1 in 20 solution of sodium in dehydrated alcohol, the latter being cooled by a stream of cold water; contains 18% of  $\text{C}_2\text{H}_5\text{ONa}$ . Rapidly becomes brown.

**Uses.** Effective caustic for nævi, warts and lupus; also in hypertrichosis. Applied with a glass rod for 2 or 3 successive days. No water should be allowed to touch the part.

**Liquor Sodii Methylatis.**

Is prepared on lines similar to the above, employing methyl instead of ethyl alcohol.

**Sodii Bicarbonas** (*B.P.*, *U.S.P. XI*, *P. Helv V*, *P. Dan.*, *etc.*).  $\text{NaHCO}_3 = 84.00$ . *Syn.* SODII CARBONAS ACIDUS, SAL DE VICHY (*F.E. VIII*).

*Dose.*—15 to 60 grains (1 to 4 g.). *U.S.P. XI* average dose 15 grains

Occurs in small white crystals or powder

**Soluble** 1 in 11 of water; insoluble in alcohol 90%.

20 parts are neutralised by 17 of citric or 18 of tartaric acid.

**Incompatible** with acids and acid salts, and with metallic and alkaloidal salts. Bismuth, magnesium and lithium benzoates and salicylates are incompatible with sodium bicarbonate. It is also incompatible with aspirin. Acetates of lead and zinc liberate  $\text{CO}_2$  from it

**Uses.** Is largely employed in dyspepsia and is of value in diabetes. A little rubbed on to the gum or placed in the cavity of a tooth may stop toothache. Large doses very useful in infantile vomiting; to neutralise the acid intoxication in these cases 100 grains are given when attack threatens, or smaller doses, *e.g.*, 10 to 15 grains every hour when an attack commences. It is given in rheumatic affections and in gastric ulcer and found of value in suppression of urine. In a normal person 2 drachms of sodium bicarbonate *per os* will usually render the urine alkaline in 24 hours. May be given intravenously in diabetic coma, 1 litre of 3 to 5% solution being administered slowly ( $\frac{1}{4}$  to  $\frac{1}{2}$  hour)

**Isotonic Sodium Bicarbonate Solution** contains 1.35% *w/v*.

**ALKALIPENIA**, with reference to acidosis as observed in children. A normal adult wants approximately 75 gr (5 g) of sodium bicarbonate to render the urine alkaline, and an infant 20 to 40 gr. In acidosis approximately 100 to 200 g are required to produce an alkaline urine. Over 200 g, death ensues — A. D. Symons, *Lancet*, i/1922, 627.

**BLACKWATER FEVER** Sodium bicarbonate intravenously, 10 to 20 ounces of strength 150 gr to the pint curtails duration of attack, prevents blockage of kidney tubules, and avoids suppression of urine — W. E. Cooke and H. Willoughby, *Lancet*, i/1929, 334.

Sodium bicarbonate orally and the citrates or lemonade. Sodium bicarbonate 10 g, glucose 10 g, given in 1000 ml initially and large amounts (up to 21 g in 24 hours) repeatedly during treatment. Quinine could be taken when the urine was kept alkaline — C. C. Chesterman, *Lancet*, i/1929, 1355. *See also* C. P. Downison, ii/1929, 47.

**BLEPHARITIS.** Sodium bicarbonate in warm 3% solution is the most generally serviceable cleansing solution in treatment of blepharitis. — R. A. Greaves, *Lancet*, ii/1923, 997

**EC/EMA.** Obstinate cases cured by daily bath of 2 lb. of sodium bicarbonate to 20 gallons of water, with change of linen and an ounce of magnesium hydrate twice daily. A case of 18 years' standing cleared up in 3 days. — S. A. Leader, *Brit. med. J.*, ii/1931, 323.

**INFLUENZA** Sodium bicarbonate 20 to 30 gr. 4 times hourly relieves abdominal pain and distension, and probably inhibits growth of the streptococcus and neutralises its toxin, the organism being in the bowel — H. O. Butler, *Lancet*, i/1922, 198.

POST-PARTUM ECLAMPSIA treated by intravenous injections of sodium bicarbonate solution.—See H. P. Wilson, *J. Amer. med. Ass.*, i/1927, 380.

PYELITIS, INFANTILE. Pyrexia in infants a few days or weeks old may often be due to pyelitis, in which sodium bicarbonate with abundant water is of use.—*Lancet*, ii/1925, 510.

**Balneum Effervescens (B.P.C.)** Sodium bicarbonate 16 oz and sodium acid sulphate 8 oz. per 30-gallon bath

**Balneum Effervescens cum Chlorido (B.P.C.)** is the same with the addition of sodium chloride 48 oz and calcium chloride 8 oz

**Bain dit de Vichy (Fr. Cx)**

Sodium bicarbonate 500 g., dissolve in the bath at time of use

**Collutorium Alkalinum Compositum.**

Sodium bicarbonate 15 gr, sodium chloride 10 gr, sodium salicylate 1 gr, thymol, menthol  $\frac{1}{2}$  gr. each, glycerin of borax 1 dr, thymol solution to 1 oz, 1 part to be used in 4 of water For post-nasal catarrh

**Collyrium Sodii Bicarbonatis (B.P.C.)** 2% w/v

**Gargarisma Sodii Bicarbonatis (B.P.C.)** 5% w/v

**Guttæ Sodii Bicarbonatis (T.H.)** Sodium bicarbonate 15 gr, phenol 1 gr, glycerin 2 dr, water to  $\frac{1}{2}$  oz. For softening wax in the ear before syringing

**Mistura Sodii Bicarbonatis Aromatica (B.P.C.)**

*Syn.* MISTURA CARMINATIVA.

*Dose.*— $\frac{1}{2}$  to 1 ounce (15 to 30 ml.)

Contains sodium bicarbonate 10 gr. per oz. with aromatic spirit of ammonia, compound tincture of cardamom, glycerin and dill water.

**Mist. Carminat. (N.I.F.)** Sodium bicarbonate 10 gr, light magnesium carbonate 5 gr., aromatic tincture of cardamom 5 m, water to  $\frac{1}{2}$  oz

**Mistura Carminativa (Gt. Orm. H.)** (*Dose* for 1 year old child)

Sodium bicarbonate  $1\frac{1}{2}$  gr., aromatic spirit of ammonia  $1\frac{1}{2}$  m, glycerin 5 m, peppermint water to 1 dr.

**Nebula Alkalina (T.H.)** Sodium bicarbonate 15 gr, borax 15 gr, phenol 4 gr, glycerin 45 m., water 1 oz. **Dobell's Solution** is approx half this strength.

**Nebula Alkalina Composita (B.P.C.)**

Sodium bicarbonate and borax of each 1.5% w/v, and phenol 0.75% w/v, in glycerin and water.

**Sodii Citro-Tartras Effervescens (B.P.C.)**

*Dose.*—1 to 2 drachms (4 to 8 g.).

Effervescent granules containing sodium bicarbonate, citric and tartaric acids.

**Tab. Nasal Alk. (N.I.F.)** Sodium bicarbonate 5 gr, thymol  $\frac{1}{10}$  gr., borax 5 gr. 1 to be dissolved in 4 tablespoonfuls of warm water.

**Tabellæ Sodii Bicarbonatis Compositæ (B.P.C.)**

*Syn.* SODA MINT TABLETS. *Dose.*—1 to 4 tablets.

Contain sodium bicarbonate 5 gr., ammonium bicarbonate  $\frac{1}{2}$  gr., saccharin and oil of peppermint.

**Tabellæ Zingiberis Compositæ (B.P.C.)** *Syn.* GINGER MINT TABLETS. *Dose.*—1 or 2 tablets.

Sodium bicarbonate 5 gr., oleoresin of ginger  $\frac{1}{10}$  gr., ammonium bicarbonate, saccharin and oil of peppermint.

**Sodii Carbonas (B.P., P. Helv. V, P. Dan., etc)**

$\text{Na}_2\text{CO}_3, 10\text{H}_2\text{O} = 286.2$ .

*Dose.*—5 to 15 grains (0.3 to 1 g.).

Rhombic crystals efflorescing in air.

**Soluble** 1 in 2 of water; insoluble in alcohol 90%.

**Uses.** Internally in gout and skin diseases and for "acidity." A lotion, 2 gr. to the ounce, relieves eczema. 1% is used as mouth wash or nasal douche. Instruments are boiled in a 1% solution to sterilise and to prevent rusting. The intravenous injection of 30 ounces of 3 to 4% solution affords best chance of restoring patient in diabetic coma, but the bicarbonate would seem preferable. A 5% solution has caused death.

**Balneum Alkalinum** (B.P.C.) contains 5 oz. of sodium carbonate per 30 gallons.

**Liquor Sodii Carbonatis** (R.L.O.H.)

To sterilise instruments sodium carbonate 1 oz., sterile water to 80 oz. Boil Graefe knives  $\frac{1}{2}$  minute, other instruments 3 minutes.

**Sodii Carbonas Exsiccatus** (B.P., P. Helv. V, P. Dan.)

$\text{Na}_2\text{CO}_3 = 106.0$

**Dose.**—2 to 5 grains (0.12 to 0.3 g.)

Approximately 106 of the exsiccated salt are obtained from 286 of the crystals.

**Sodii Carbonas Monohydratus** (U.S.P. XI, P. Helv. V).

$\text{Na}_2\text{CO}_3 \cdot \text{H}_2\text{O} = 124.0$ . U.S.P. XI average dose 4 grains. Is known in commerce as concentrated "crystal soda," and used as a bath salt and water softener. It occurs in small silky crystals.

**Sodii Sesquicarbonas.**  $\text{Na}_2\text{CO}_3 \cdot \text{NaHCO}_3 \cdot 2\text{H}_2\text{O}$  In silky crystals or as a white powder. Is sometimes used in the preparation of bath salts.

**Sodii Chloras** (B.P.C., F.E. VIII)  $\text{NaClO}_3 = 106.5$ .

**Dose**—5 to 10 grains (0.3 to 0.6 g.)

**Caution.** Not to be rubbed with combustible substances. Colourless crystals or crystalline powder with saline taste, soluble 1 in less than 2 parts of water, about 1 in 100 of alcohol 90%, and 1 in 5 of glycerin.

Used in diphtheria, stomatitis, sore throat, and in urethritis. It is used in some non-poisonous weed-killers.

If salivation shows itself in mercurial treatment of syphilis, sodium chlorate or potassium chlorate mouth-wash, or sodium chlorate internally 10 to 20 grains best.—W. Knowsley Sibley, *Prescriber*, 1921, 162.

[P2 87] **Sodii Hydroxidum** (B.P., U.S.P. XI, P. Helv. V, P. Dan.).  $\text{NaOH} = 40.00$  Syn. SODA CAUSTICA.

[P2] "Sodium hydroxide."

[83] "Sodium hydroxide—in substances containing less than twelve per cent. of sodium hydroxide"

[86] "Sodium hydroxide—specify proportion as the proportion of sodium monoxide ( $\text{Na}_2\text{O}$ ) which the preparation would be calculated to contain on the assumption that the sodium hydroxide in the preparation had been wholly converted into sodium monoxide."

[87] Sodium hydroxide and articles containing it must be labelled "Caution. This substance is caustic."



**Dose.**— $\frac{1}{2}$  to 1 grain (0.03 to 0.06 g.) well diluted.

In fused masses, moulded sticks or white scales, containing not less than 95% of total alkali calculated as NaOH. U.S.P. XI requires minimum of 95% of total alkali of which not more than 3% is  $\text{Na}_2\text{CO}_3$ .

**Antidotes.** Treat as for poisoning by ammonia, see p. 170.

Eight cases of poisoning (4 suicides) in Cyprus during 1933 with 6 fatalities. The fatal dose varied from 5 to 60 grammes. It is largely used for domestic washing purposes.—S. G. Willmott and M. Gosden, *Brit. med. J.*, 1/1934, 1022. See also *Lancet*, 11/1933, 413.

**Sodii Nitris** (B.P., U.S.P. XI, P. *Helv.* V).  $\text{NaNO}_2 = 69.0$ .

**Dose.**— $\frac{1}{2}$  to 2 grains (0.03 to 0.12 g.) U.S.P. XI average dose 1 grain. P. *Helv.* V has max. single dose approx.  $1\frac{1}{2}$  grains, max. in 24 hours approx. 5 grains.

Is obtained by reduction of sodium nitrate by fusing it with lead.

In white or slightly yellow deliquescent, crystalline granules, with a cooling saline taste.

**Soluble** 1 in  $1\frac{1}{2}$  of water, 1 in 50 of alcohol 90%.

**Antidotes.** Treat as for poisoning by amyl nitrite, see p. 151.

Deaths of three members of one family at Middlesbrough 2 hours after consuming sodium nitrite used in error for salt. The first fatal case of nitrite poisoning in this country.—*Pharm. J.*, ii/1936, 214.

**Uses.** In angina pectoris and in epileptiform convulsions—action similar to amyl nitrite. For asthma 3 to 5 grains frequently repeated; specially useful with hyoscyamus. Valuable in granular kidney; high tension of the pulse is natural to the disease. Raised arterial tension when dangerous is well treated by  $\frac{1}{2}$ -grain doses, gradually increased to 4 or 5 grains. Attacks of asthma may be warded off by sodium nitrite  $\frac{1}{2}$  gr. with sodium iodide 3 gr. taken (e.g. in a tablet) every 2 or 3 hours. A 2-gr. dose of sodium nitrite with 3 gr. of sodium iodide has been advocated for paroxysmal pain due to aortic insufficiency.

It does not fulfil the requirements of the treatment of arterial hypertension in that it has no constant and sustained action, does not act by dilating the arterioles all over the constricted areas, may give rise to unpleasant symptoms and side-effects, does not maintain the normal functions of the heart and kidneys, and may depress renal activity.—S. Weiss and L. B. Ellis, per *Brit. med. J. Ept.*, 11/1933, 72.

[P1] **Tabellæ Sodii Nitritis Compositæ** (G. Oliver)

**Dose.**—1 or more as required.

Sodium nitrite  $\frac{1}{2}$  gr., diluted erythrityltetranitrate  $\frac{1}{2}$  gr., mannitol nitrate  $\frac{1}{2}$  gr., ammonium hippurate 1 gr. See also **Pulvis Potassii Nitritus Compositus** and **Pulvis Sodii Nitritus Compositus**.

**Liquor Æthylis Nitritus** (B.P.C.).

**Dose.**— $\frac{1}{4}$  to 1 drachm (1 to 4 ml.). Should be directed to be added to a small quantity of water at the time of taking.

A solution of ethyl nitrite, 2.5 to 3% w/w (equivalent to 2 to 2.5% w/v) in a mixture of dehydrated alcohol and glycerin.

**Spiritus Ætheris Nitrosi** (B.P.).

**Syn.** SWEET SPIRIT OF NITRE.

**Dose.**—15 to 60 minims (1 to 4 ml.)

An alcoholic solution containing ethyl nitrite (1.25 to 2.5%

*w/v*), aldehyde and other substances. *P. Helv. V* requires 2.0 to 2.5% *w/v*.

Any loss of strength in this is generally due to volatilisation of the ethyl nitrite alone. Only direct sunlight has any effect in inducing decomposition, and this can be prevented by storing in amber bottles with greased stoppers.—*R. Wright, Pharm J.*, i/1926, 256

**Incompatible** with potassium iodide, also with phenazone unless previously neutralised with sodium bicarbonate; also incompatible with salicylates and ferrous sulphate

**Uses.** Antipyretic, diaphoretic, diuretic, and stimulant. Relieves the spasm and pain of asthma, dysmenorrhœa, angina pectoris, also the pain of the passage of renal calculi and gall-stones.

**Spiritus Æthylis Nitritus** (*U S P XI*) Average dose—30 minims (2 ml)  
An alcoholic solution containing 3.5 to 4.5% *w/w* of  $C_2H_5ONO$

## STRAMONIUM

*B P., U.S.P. XI, etc.*

[P1] "*Alkaloids, the following, their salts, simple or complex:—atropine; hyoscyne, hyoscyamine; solanaceous alkaloids not otherwise included in this List.*"

[81] "*Alkaloids, the following; their salts, simple or complex:—Atropine except substances containing less than 0.15% of atropine, hyoscyne except substances containing less than 0.15% of hyoscyne; hyoscyamine except substances containing less than 0.15% of hyoscyamine; solanaceous alkaloids not otherwise included in this Schedule, except substances containing less than 0.15% of solanaceous alkaloids calculated as hyoscyamine.*"

[83] "*Alkaloids—Solanaceous alkaloids—in stramonium contained in preparations for the relief of asthma in the form of cigarettes, smoking mixtures or fumigants*"

[86] "*Alkaloids—Solanaceous alkaloids not otherwise included in the Poisons List—specify proportion as the proportion of any one of the solanaceous alkaloids that the preparation would be calculated to contain on the assumption that all the solanaceous alkaloids in the preparation were that alkaloid.*"

**Dose.**— $\frac{1}{2}$  to 3 grains (0.03 to 0.2 g.); 3 grains contains about  $\frac{1}{10}$  gr. of alkaloids *U.S.P. XI* average dose  $1\frac{1}{2}$  grains *P. Helv. V* has max. single dose approx 5 grains, max. in 24 hours approx 15 grains.

Dried leaves and flowering tops of *Datura Stramonium* (syn. THORNAPPLE) and of *D. tatula* (Solanaceæ) containing not less than 0.25% of alkaloids calculated as hyoscyamine.

*U.S.P. XI* requires not less than 0.3% of alkaloids. *F.E. VIII* not less than 0.25%. *P. Helv. V* not less than 0.2%.

It contains about 0.25 to 0.5% of alkaloids, chiefly hyoscyamine, together with atropine and hyoscyne

A key for distinguishing various species of *Datura*—H. A. Timmerman *Pharm J.*, i/1927, 574.

**Antidotes.** Treat as for poisoning by atropine, see p. 228.

**Uses.** Its action is similar to that of belladonna, and it is employed for the same purposes. Is a usual ingredient in cigarettes and fumigating powders employed in asthma Tincture and extract of stramonium have been used in parkinsonism.—*v. postea.*

PARKINSONISM has been treated by stramonium in pills or cachets, in progressively increasing doses of 0.05 or 0.10 g. to limit of tolerance, given preferably during meals. To avoid habituation, administer for 20 days with intervals of 10 days.—*Brit med J. Ept.*, 1/1926, 56

Chronic encephalitic parkinsonism. Results equal to those from hyoscine hypodermically are obtained by giving stramonium extract *per os* in dose of 0.25 g. to 1 g. or more thrice daily, the average dose being 0.75 g. Similar results obtained from Ext Stramon Exsicc (B.P.C.), stramonium leaves, and the tincture. The leaves have disadvantage of excessive bulk. Therapeutically it was found that 180 gr. of hyoscine hypodermically = dried leaves 1 g. = Ext Stramon 0.25 g = Ext Stramon Exsicc 0.25 g = Tinct. Stramon 3 dr. No actual curative effect is possible. Palliative treatment essential. The value of hyoscine in idiopathic paralysis agitans was shown by Erb in 1906. Chronic encephalitic parkinsonism is similar clinically. *Per os* medication needed to replace irksome routine of 3 hypodermic injections daily. 80 cases were on the extract for 6 months. Many were in a satisfactory condition on 0.5 g. thrice daily. One or two were getting more than 1 g., the largest dose being 1.375 g. thrice daily. It is evident that the doses of tincture hitherto used by others for the purpose were far too small.—C. Worster-Drought and T. R. Hill, *Lancet*, 1/1930, 1225

45 to 60 minims of B.P. tincture thrice daily increases ability to perform rapid movements. Mental condition improved. May be continued for long period.—E. A. Carmichael, *per Prescriber*, 1929, 224

If there is interruption of the treatment for even a short time it is necessary to resume with small doses and work up to the maximum (0.25 g. *t d s*).—W. S. Hall, *Lancet*, 1/1934, 595

Marked improvement in the muscular rigidity of post-encephalitic parkinsonism follows the administration of large doses of stramonium combined with pilocarpine to relieve dryness of the mouth. No effect on the tremors. Give 15 m. of Tinct. Stramonii in  $\frac{1}{2}$  oz. of water on waking, after lunch and tea, if the stiffness causes disturbed nights, give another dose at bedtime. All doses of the dilution are increased by 1 drachm on alternate days until the patient complains of dryness of the mouth. Pilocarpine nitrate  $\frac{1}{16}$  gr. is then added to the latest dose of stramonium, and the dose is prescribed in  $\frac{1}{2}$  oz. of water. 1 drachm is again added to each of the doses on alternate days until sufficient relief is obtained or toxic effects (commonly slight paralysis of accommodation) are observed. Finally a prescription is given for the full dose of stramonium (generally at least 60 m.) and pilocarpine nitrate in a single  $\frac{1}{2}$  oz. of water.—A. F. Hurst, *Pharm. J.*, 11/1934, 704

Pilocarpine is not essential, it may be omitted, and that dose of stramonium alone administered which has been found best suited to the needs of the patient.—H. Stott, *Indian med. Gaz.*, 1935, 620

[P1-81] **Extractum Stramonii (B.P.C.)**

**Dose.**— $\frac{1}{4}$  to 1 grain (0.016 to 0.06 g.).

A soft extract containing 1% of alkaloids.

In spasmodic asthma the extract is found better than the tincture. Sufficient should be given to be slightly toxic. Most patients show toxic effects on taking  $\frac{1}{2}$  grain in 24 hours.

[P1-81] **Extractum Stramonii (U.S.P. XI).** **Average Dose.**— $\frac{1}{2}$  grain (0.02 g.).

In two forms, pilular and powdered extract, containing 1.20% of alkaloids, it is, therefore, about 20% stronger than the dry extract of the B.P. *Addendum* and the soft extract of the B.P.C.

[P1] **Extractum Stramonii Liquidum (B.P. Add.)**

**Dose.**— $\frac{1}{2}$  to 3 minims (0.03 to 0.2 ml.)

Adjusted to contain 0.25% of alkaloids; 3 minims contains about  $\frac{1}{180}$  grain.

[P1 81] **Extractum Stramonii Siccum** (B.P. Add.).

*Dose.*— $\frac{1}{4}$  to 1 grain (0.015 to 0.06 g.). In post-encephalitic and similar conditions, 1 to 8 grains (0.06 to 0.5 g.).

A dry granular extract prepared with alcohol 95%. Contains 1% of alkaloids.

[P1] **Tinctura Stramonii** (B.P. Add.).

*Dose.*—5 to 30 minims (0.3 to 2 ml.); 30 minims contains about  $\frac{1}{10}$  gr of alkaloids.

Prepared by dilution of the liquid extract 1 in 10 with alcohol 45%. It is approximately half the strength of the B.P. '14 tincture.

ASTHMA Tinct Stramonii 15 to 20 m thrice daily is a maximum dose. Tinct Hyoscyami 20 m combined with an intestinal antiseptic, is most potent in controlling the abnormal muscular activity, and arresting the mental symptoms in "spastic" conditions of the colon, but will cause dryness of the throat. Warning regarding large doses of Tinct Stramonii.—T Stacey Wilson, *Lancet*, 11/1930, 107

[P1] **Tinctura Stramonii** (U S P XI). *Average dose*—12 minims (0.75 ml.). 1 in 10 and standardised to contain 0.03% of alkaloids.

[P1] **Unguentum Stramonii** (B P C.) contains 10% of extract of stramonium.

[P1 81] **Stramonii Semen** (B P C, P Helv V) *Syn* THORNAPPLE SEED. The seeds of *Datura Stramonium*, containing an average of 0.2% of alkaloids.

[P1 81] **Daturæ Folium** (B P.C.). The dried leaves of *Datura Metel* (from India) and of *D. innoxia* (from Mexico and India, and cultivated in England) (Solanaceæ). Contains about 0.25 to 0.55% of hyoscyne, with traces only of hyoscyamine and atropine. Used in India for the same purposes as stramonium.

*Datura* poisoning is common in Cairo. Symptoms are those of belladonna poisoning. Writer has never seen a fatal case, though many remained on verge of death for hours.—*Lancet*, 11/1921, 1065.

[P1 81] **Daturæ Semen** (B P C) The dried seeds of *D Metel*, containing about 0.2% of hyoscyne

[P1] **Tinctura Daturæ Seminis**. *Dose*—5 to 15 minims (0.3 to 1 ml) Sedative for asthmatic cough

[P1 81] **Daturine**, *dose*— $\frac{1}{10}$  to  $\frac{1}{20}$  grain (0.0005 to 0.001 g), is a mixture of alkaloids from *Datura Stramonium* consisting chiefly of hyoscyamine with some atropine. Occurs in white crystals slightly soluble in water, freely soluble in alcohol 90%, chloroform and ether. Occasionally used as a mydriatic

## STROPHANTHUS

B.P., F.E. VIII, P. Ital V, P. Belg IV, P.G. VI, P. Helv V,  
P. Dan.

*Syn.* STROPHANTHI SEMINA

[P1] "*Strophanthus; glycosides of strophanthus.*"

"Ouabam."

[81] "*Strophanthus, glycosides of.*"

"Ouabain."

[88] "*Strophanthus, glycosides of—specify proportion as the amount of Standard Tincture of Strophanthus as defined in the British*

*Pharmacopœia which possesses the same activity as a specified quantity of the preparation when assayed by the method described in the said Pharmacopœia."*

**Dose.**—No dose is given in B.P.

The dried ripe seeds of *Strophanthus Kombé* (Apocynaceæ) freed from the awns, of a fawn colour, and covered with hairs.

*P. Ital.* includes *S. hirsutus*, and *F.E. VIII* and *P. Belg.* include also *S. gratus*, the last mentioned includes that variety under a separate heading. *P.G. VI* mentions only *S. gratus*.

**Antidotes.** Treat as for poisoning by digitalis, see p. 441.

**Uses.** As a cardiac tonic and diuretic. Resembles digitalis in effects but acts far more promptly. It is stated that the tincture acts in from  $\frac{1}{2}$  to 1 hour, while digitalis tincture takes from 24 to 48 hours. Occasionally of service where the latter has failed or is not tolerated. Especially valuable in mitral stenosis, but unsuitable in aortic disease, pulse improves in force and rhythm, dyspnœa and palpitation are lessened, appetite is increased while action of bowels and perspiration are not affected. It is non-cumulative. Of value in renal insufficiency. It is a better diuretic than digitalis because, while it accelerates the circulation, it does not readily constrict the renal vessels.

[P1 81] **Extractum Strophanthi** (B.P.C.)

**Dose.**— $\frac{1}{4}$  to 1 grain (0.016 to 0.065 g.).

A dry extract mixed with lactose, so that 2 parts of extract in powder = 1 part of seeds

[P1 81] **Tinctura Strophanthi** (B.P.)

**Dose** —2 to 5 minims (0.12 to 0.3 ml.)

Prepared by percolation with 70% alcohol of seeds defatted with light petroleum. The strength is adjusted to be equivalent to that of a 0.42% w/v solution of international standard ouabain or of a 0.33% w/v solution of anhydrous ouabain, the comparison being made by the frog method

*P. Ital. V, F.E. VIII, P. Belg. IV, Fr. Cx, and I.I.* have 1 in 10. *Fr. Cx* has max. single dose 3 minims; max. during 24 hours 12 minims approx.

[P1 81] **Strophanthinum** (B.P., U.S.P. XI) *Syn* KOMBÉ STROPHANTHIN, K-STROPHANTHIN

**Dose.**—By intramuscular or intravenous injection,  $\frac{1}{10}$  to  $\frac{1}{50}$  grain (0.00025 to 0.001 g.). *U.S.P. XI* average daily dose, intravenously  $\frac{1}{10}$  grain. It is irritating at the site of injection

Given by the mouth it is often ill tolerated and strychnine (1 to 3 mg. in the day) is the best antidote. Signs of overdose, *viz.*, headache, sense of tightness in the chest and præcordia, marked slowing of pulse or coupling of the beats, marked rise in blood pressure, cardiac arrhythmia, insomnia and nausea, are least seen with the intravenous use of the substance.

A mixture of glycosides from *strophanthus*, adjusted by admixture with lactose so as to possess 40% (*U.S.P. XI* 40 to 60%) of the activity of anhydrous ouabain

**Solubility.** The undiluted mixture of glycosides is moderately soluble in water and in alcohol 90%, less soluble in dehydrated alcohol, sparingly soluble in chloroform, almost insoluble in ether, benzene and light petroleum.

**Contraindicated** where there is a high blood pressure and marked arteriosclerosis, and in those with acute or chronic nephritis or granular kidney.

There is no degree and no phase of cardiac insufficiency from the beginning of the disease—often difficult to gauge—to the stage of extreme abnormality in the distribution of blood, along with its accompaniments, which does not respond to the intravenous administration of strophanthin. Only the compensated heart on the one hand or the dying heart on the other not yet responds or no longer responds to this treatment. The prognosis of cardiac insufficiency has entirely changed since the possibility has arisen through the use of strophanthin not only of enlarging the field in which treatment with digitalis is indicated, but also of making success in the treatment of certain cases more assured. The heroic treatment of heart failure with calomel and digitalis by mouth is now replaced by one which involves the administration of mersalyl, and so supplements the effect of strophanthin in this disease. The appropriate combination of both remedies, not simultaneously or on the same day even, but one after the other on different days, makes possible the removal of oedema of the severest degree as well as that of very long standing—A. Fraenkel, *Lancet*, ii/1935, 1104.

[P1 81] **Granules de Strophanthine** (*Fr. Cx.*),  $\frac{1}{10}$  mg. in each, coloured pink. [P1 81] **Poudre de Strophanthine au Centième** (*Fr. Cx.*). Max. single dose  $\frac{1}{2}$  grain; max. during 24 hours  $1\frac{1}{2}$  grains approximately.

[P1 81] **Kombetin** (*Boehringer, Mannheim; Pharmaceutical Products, London*) Glycoside from *Strophanthus Kombé*. Ampoules of 1 ml. = 0.0005 g. Dose.—Initially 0.00025 g. intravenously, 0.0005 g. as average dose in 24 hours.

[P1 81] **Strophanthone** (*Parke, Davis, London*) Preparation of the active principles of *Strophanthus Kombé* seed for oral use. Dose.—2 to 10 minims.

[P1 81] **Strophanthone Dilute** (*Parke, Davis, London*). Preparation of *Strophanthus Kombé* seed in ampoules for hypodermic or intravenous administration. Dose.—Hypodermically, 1 ml. initially, subsequently as required. Intravenously, 0.5 ml.

[P1 81] **Ouabainum.**  $C_{30}H_{48}O_{13}, 9H_2O = 760.5$ . Syn G-STROPHANTHIN, STROPHANTHINUM (*P.G. VI, P. Dan.*).

Dose.— $\frac{1}{10}$  to  $\frac{1}{80}$  grain (0.00025 to 0.001 g.), by injection. *P.G. VI* max. single dose  $\frac{1}{10}$  grain; max. daily dose  $\frac{1}{12}$  grain.

Obtained from *S. gratus* seeds, also present in wood of *Acokanthera Schimperii* (*Apocynaceæ*). Is about twice as toxic as K-strophanthin, and is used as an international standard for control of the standard preparation of strophanthin which is used for the biological assay of strophanthin and strophanthus preparations.

## STRYCHNINA

*B.P.C., Fr. Cx., F.E. VIII*

$C_{21}H_{22}O_2N_2 = 334.2$ .

[P1] "Alkaloids, the following; their salts, simple or complex:—*Strychnine*."

[81] "Alkaloids, the following; their salts, simple or complex:—*Strychnine* except substances containing less than 0.2 per cent. of *strychnine*."

*Rule 15 of the Poisons Rules, 1935, prohibits the sale or supply of strychnine (or its salts) except in certain circumstances, see page 989.*

**Dose.**— $\frac{1}{32}$  to  $\frac{1}{8}$  grain (0.002 to 0.008 g.). *Fr. Cx.* has max. single dose  $\frac{1}{16}$  grain; max. during 24 hours  $\frac{1}{4}$  grain approx.

The alkaloid obtained from *nux vomica*, St. Ignatius' beans (*q.v.*), and the seeds of other species of *Strychnos*. In characteristic colourless crystals. Exceedingly poisonous. Its absorption from the rectum is even more rapid than from the stomach, small intestine, œsophagus or colon.

It is supplied pink to cover brown tint forming in hot climates

**Soluble** 1 in 7000 of water, about 1 in 400 of alcohol 60%, 1 in 150 of alcohol 90%, 1 in 350 of dehydrated alcohol, 1 in 6 of chloroform, nearly insoluble in ether.

**Antidotes.** If patient is seen at once, empty stomach by emetics or stomach tube, but if tetanic symptoms have already set in, first give chloroform as anæsthetic and then use the stomach tube with a solution of 60 gr. of potassium permanganate in 2 gallons of water. Give medicinal charcoal, stirred up in water, freely.

(Some authorities say that emetics and the stomach tube must not be used or fatal convulsions may be caused. Give potassium permanganate in 10 gr. doses, or medicinal charcoal.)

Keep patient lying down and quiet, fully under chloroform if necessary. If convulsions persist, give potassium bromide 4 dr., and chloral hydrate 30 gr., repeating every hour if necessary. Soluble barbitone, soluble phenobarbitone or sodium Amytal intravenously considered of value. Saline with dextrose infusion. Artificial respiration and inhalations of oxygen with 7% carbon dioxide.

Efficacy of sodium Amytal injected intravenously in strychnine poisoning.—Stalberg and Davidson, *J. Amer. med. Ass.*, 11/1933, 102

Pentobarbital sodium less effective in antidotal action than sodium Amytal for strychnine poisoning in rabbits.—Swanson, *J. Amer. pharm. Ass.*, 1935, 959

6 gr. of strychnine hydrochloride taken for suicidal purposes; patient given 30 gr. of zinc sulphate within 20 minutes, chloroform anæsthesia and  $\frac{1}{4}$  gr. morphine hypodermically. He became cyanosed, was given amyl nitrite, gastric lavage with potassium permanganate solution, some left in stomach. Later morphine and atropine given, chloral hydrate and potassium bromide by rectum, more morphine and atropine. Anæsthesia maintained, amyl nitrite repeated, also chloral and bromide. Oxygen with carbon dioxide administered for  $\frac{1}{4}$  hour. Spasms diminished, cyanosis lessened, respiration improved, patient drank water, slept, vomited and was discharged well next day. Severe asphyxia was not relieved by chloroform anæsthesia with morphine until amyl nitrite also given — *Brit. med. J.*, 1/1936, 363

Poisoning in U.S.A. caused 546 deaths from 1926 to 1928, compared with 11 for England and Wales for 1930 to 1931. One-third of the accidental poison deaths occur in children under 5 years of age, due to the popularity of "tonic" tablets containing strychnine.—*Brit. med. J.*, 11/1932, 159.

**Uses.** Given orally strychnine acts as a bitter stomachic, causing increased secretion of gastric juice. It raises blood pressure and is a useful circulatory tonic in cardiac failure, especially when given hypodermically. In combination with expectorants it is a respiratory stimulant in acute bronchitis and pneumonia

For old people, strychnine and nux vomica have been described as the only useful bitter tonics.

Strychnine has a powerful action on the vasomotor system and stimulates the liberation of adrenaline. It has no direct cardiac action of value but acts through the adrenaline—O. S. Gibbs, *Brit. med. J.*, i/1931, 582

[P1 81] **Ferri et Strychninæ Citras (B.P.C.).**

*Dose.*—1 to 3 grains (0.06 to 0.2 g.).

In deliquescent green scales, freely soluble in cold water. It contains 1% of strychnine, and about 13% of Fe.

[P1 81] **Ferri, Quininæ et Strychninæ Citras.**

*Dose.*—2 to 5 grains (0.12 to 0.3 g.).

Similar to the former, with about 15% of quinine. In deliquescent scales, soluble 1 in 2 of water.

[P1 81] **Strychninæ Arsenas.**  $C_{21}H_{21}O_2N_3, H_3AsO_4, \frac{1}{2}H_2O = 485.1$ .

*Dose.*— $\frac{1}{4}$  to  $\frac{1}{2}$  grain (0.001 to 0.004 g.)

In small white acicular crystals containing 68.7% of strychnine, soluble 1 in 14 of water.

In phthisis by hypodermic injection of  $\frac{1}{2}$ % mixture with liquid paraffin. *Dose.*—4 to 15 minims daily.

In addition to this acid salt there is another of composition—

$C_{21}H_{21}N_3O(H_3AsO_4)_2, H_2O$ . It contains much less strychnine (42.8%)

[P1 81] Strychnine acetate is soluble 1 in 44, the [P1 81] **hydrobromide** 1 in 70, the [P1 81] **hypophosphite** (one of the most soluble salts) 1 in 33

[P1 81] **Strychninæ Hydrochloridum (B.P.)**

$C_{21}H_{22}O_2N_3, HCl, 2H_2O = 406.7$ .

*Dose.*— $\frac{1}{32}$  to  $\frac{1}{8}$  grain (0.002 to 0.008 g.),

Small trimetric prisms, soluble 1 in 35.5 of water; 1 in about 80 of alcohol 90%.

A 1% w/v solution is strongly hypotonic, 0.079 g. of sodium chloride or 0.442 g. dextrose to every 10 ml. renders it isotonic.

[P1 81] **Injectio Strychninæ (B.P.C.).**

*Dose.*—5 to 10 minims (0.3 to 0.6 ml.), by hypodermic injection

Contains 0.75% w/v of strychnine hydrochloride, 10 minims contains about  $\frac{1}{16}$  grain.

[P1 81] **Liquor Strychninæ Hydrochloridi (B.P.)**

*Dose.*—3 to 12 minims (0.2 to 0.8 ml.); 12 minims contains about  $\frac{1}{8}$  gr. of strychnine hydrochloride.

Strychnine hydrochloride 1, alcohol (90%) 25, water to 100.

**Incompatible** with alkalis, e.g., sodium bicarbonate, sal volatile, bromides and iodides.

It is safer to prescribe tincture of nux vomica in preference to solution of strychnine hydrochloride when there is danger of incompatibility.

[P1] **Mist. Acid. c. Strych. (N.F.).** Dilute hydrochloric acid 10 m., solution of strychnine hydrochloride 3 m., chloroform water to  $\frac{1}{2}$  oz.

[P1 81] **Strychninæ Nitras (B.P.C., U.S.P. XI, P.G. VI, P. Belg. IV, P. Hung., P. Helv. V, P. Dan., P. Ital. V, F.E. VIII).**

$C_{21}H_{22}O_2N_3, HNO_3 = 397.2$ .

*Dose.*— $\frac{1}{32}$  to  $\frac{1}{8}$  grain (0.002 to 0.008 g.). *P. Helv. V* and *P. Hung.* give max. single dose  $\frac{1}{8}$  grain; max. in 24 hours  $\frac{1}{4}$  grain. *P.G. VI* gives half these amounts; *F.E. VIII*  $\frac{1}{80}$  and  $\frac{1}{16}$  grain respectively. *U.S.P. XI* average dose  $\frac{1}{16}$  grain.



Colourless needles, soluble 1 in 60 of water (1 in 45 at 25°—*U.S.P. XI*), 1 in 120 of alcohol 90%.

[P1-81] **Injectio Strychninæ, Arseni Iodidi et Quininæ.** Strychnine nitrate 1 gr., arsenic triiodide 2 gr., quinine lactate 1 dr., distilled water to 3 oz

*Dose.*—Up to 1 drachm hypodermically for adults.

Specific to reduce temperature in influenza attacks and almost any grave affection. Also prophylactic, *e.g.*, in malaria.

[P1-81] **Strychninæ Sulphas** (*B.P.C.*, *U.S.P. XI*, *Fr. Cx.*, *F.E. VIII*, *P. Ital. V*). ( $C_{21}H_{22}O_4N_2$ )<sub>2</sub>.H<sub>2</sub>SO<sub>4</sub>.5H<sub>2</sub>O = 856.5.

*Dose.*— $\frac{1}{32}$  to  $\frac{1}{8}$  grain (0.002 to 0.008 g.). *Fr. Cx.* has max. single dose  $\frac{1}{10}$  grain; max. during 24 hours  $\frac{1}{4}$  grain approx. *F.E. VIII*  $\frac{1}{10}$  and  $\frac{1}{7}$  grain respectively. *U.S.P. XI* average dose  $\frac{1}{10}$  grain.

The neutral salt is in prismatic crystals, soluble 1 in 62 of water and 1 in 135 of alcohol 90%. M. p. 200°. It contains  $5\frac{1}{2}H_2O$ , *i.e.*, there is usually a loss on drying of 11.44% approx.

[P1-81] **Hypodermic Injection** 1 in 100. *Dose.*—1 to 6 minims

[P1-81] **Strychninæ Sulphas Acidus** *Syn.* HULLF'S SOLUBLE STRYCHNINE.  $C_{21}H_{22}O_4N_2$ .H<sub>2</sub>SO<sub>4</sub>.2H<sub>2</sub>O = 468.3.

*Dose.*— $\frac{1}{84}$  to  $\frac{1}{10}$  grain (0.001 to 0.004 g.)

In white silky acicular crystals with a slightly acid reaction, soluble 1 in 42 of water.

[P1-81] **Strychninæ Valerianas.**

A non-crystallisable salt supplied in aqueous solution equivalent to 25% of the base *Dose.*— $\frac{1}{2}$  minim to  $\frac{1}{4}$  minim (=  $\frac{1}{16}$  to  $\frac{1}{8}$  grain of the base) A useful nervine tonic.

**Brucine.**  $C_{23}H_{26}O_4N_2.4H_2O$  = 466.3

[P1] "*Alkaloids, the following; their salts, simple or complex — Brucine.*"

[81] "*Alkaloids, the following, their salts, simple or complex:— Brucine except substances containing less than 0.2 per cent. of brucine.*"

*Dose.*— $\frac{1}{16}$  to  $\frac{1}{8}$  grain. An alkaloid from *Strychnos Nux Vomica* seeds—small white acicular crystals, with bitter taste. Very soluble in alcohol and chloroform. Its salts are soluble in water.

It is said to possess only  $\frac{1}{10}$  of the physiological power of strychnine. For epilepsy the [P1-81] hydrochloride,  $C_{23}H_{26}O_4N_2.HCl$  = 430.7, has been given as liquor, same strength as Liquor Strychninæ, in 10-minim doses increased until  $\frac{1}{8}$  grain is reached [P1-81] Brucine sulphate ( $C_{23}H_{26}O_4N_2$ )<sub>2</sub>.H<sub>2</sub>SO<sub>4</sub> = 686.5 + Aq. White crystals soluble 1 in 80 in water.

[P1-81] **Curara** (*B.P.C.*). *Syn.* CURARE, OURARI, URARI, WOURARA, WOURALI.

[P1] "*Alkaloids, the following; their salts, simple or complex:— Curarine.*"

[81] "*Alkaloids, the following; their salts, simple or complex:— Curarine.*"

*Dose.*— $\frac{1}{10}$  to  $\frac{1}{8}$  grain (0.003 to 0.03 g.).

Curare, the South American Indian arrow poison, is an extract of different plants of which the active principle is derived from the bark of various kinds of a liana-like South American *Strychnos*. Commercial "calabash" curare is derived from *S. toxifera*. "pot" curare from *S. Castelnæi* together

with *Cocculus toxiferus* (Menispermaceæ), while "tube" curare is from unknown plants.

It is a blackish-brown dry extract, with bitter taste; contains some resin but is nearly all soluble in water

Use of wourah as arrow poison in South America—Sir J. Bland-Sutton, *Brit. med. J.*, ii/1922, 932.

Tetanus treated by curare after antitoxin had failed. Subcutaneous injections of 2, increased daily to 5 mg. An attempt to raise the dose to 6 mg. led to transient paralysis of the respiratory muscles, causing dyspnoea. The dose of 5 mg was continued. The convulsions which sometimes occurred every hour subsided. Patient received 63 mg in 14 days—*Brit. med. J. Ept*, i/1921, 93.

[P181] **Curarina.**  $C_{15}H_{25}ON_2 = 298.2$ .

The active principle of gourd curare is a powerful poison, in yellowish powder soluble in water and in alcohol. The drug also contains curine, identical with beberine. Bamboo (tube) curare and pot curare contain allied alkaloids.

A case of tetanus successfully treated by curarine in conjunction with anti-tetanic serum intravenously. A sterile solution of curarine hydrochloride (free from curine) containing 1 mg. in 1 ml. was prepared freshly every few days and given subcutaneously; initial dose 0.1 mg. repeated 4-hourly, the size of dose and frequency of administration being slowly increased daily until 8 doses of 0.5 mg. were being given in 24 hours. In all, 48.1 mg. of curarine were given in 20 days.—J. S. Mitchell, *Lancet*, i/1935, 262.

Curarine treatment of tetanus should still be reserved for cases which are already very severe or in which, by the accepted criteria, the prognosis is very grave. The best method of giving it is by the intravenous drip, using curarine chloride in solution, 100 mg. of the solid to a pint of saline or glucose saline, and adjusting the inflow so as to deliver 0.25 mg. per kg. of bodyweight per hour to the patient, arranged so as to be equivalent to about 30 drops per minute in the drip. A pint of solution lasts about 6½ hours. At first the solution is run in at 6 times its maintenance rate, so that 0.25 mg. per kg. is delivered in about 10 minutes; this should be sufficient for curarisation. During this period and for the first hour following administration at maintenance rate its effects should be closely watched, since a real danger of curarine treatment is the sudden onset of bronchial spasm. Animal experiments justify the administration of atropine, ½ to 1 gr. hypodermically before and at 4-hour intervals during the period of curarisation, and a full dose of adrenaline if the spasm occurs. Curarine in its present form is unsuitable for treatment of cases of chronic rigidity, and is given in tetanus only as a means of removing muscular spasm—antitoxin is required as urgently as with any other treatment—R. West, *Lancet*, i/1936, 12.

**Ibogaïne.**  $C_{23}H_{35}O_2N_2 = 386.6$ . An alkaloid obtained from the Iboga (*syn* aboua, obouete, or liboka) *Tabernanthe Iboga* (Acanthaceæ), a plant growing in West Africa, particularly the Congo. Said to have aphrodisiac and sustaining powers. Too large a dose may produce tetanus and convulsions. The plant has been tried in sleeping sickness. The base is soluble 1 in 28 of alcohol 95%, insoluble in water. It has been given in dose 0.005 g. (½ grain). **Ibogaïne Hydrochloride** has been given in influenza, and in angina pectoris and other heart affections.

**Muira-Puama.** This drug, which comes from Brazil, has been described as belonging to *Liriosma ovata* (Olacaceæ). It is said to contain an alkaloidal crystalline substance, an amorphous bitter substance, a little fat, and two kinds of resinous acids. Brazilian drugs vary, however. It has an irritating action, also tonic aphrodisiac properties. Used in nervous disorders.

[P181] **Muimbin** (Paines & Byrne, London). A combination of muira-puama and yohimbine hydrochloride. Dose.—1 or 2 tablets at night. Sexual impotence.

**Pilula Potentini Composita** (Martindale, London). Muira-puama extract 1 gr., with ovolecithin 1 gr. Dose.—3 to 6 daily before meals. A nerve stimulant and aphrodisiac.

[P1-81] **Picrotoxinum** (B.P.C., Fr. Cx.).  $C_{30}H_{34}O_{13} = 602.3$ .

[P1] "*Picrotoxin.*"

[81] "*Picrotoxin.*"

*Dose.*— $\frac{1}{100}$  to  $\frac{1}{25}$  grain (0.0006 to 0.0025 g.)

Colourless odourless crystals or microcrystalline powder extracted from *cocculus indicus*. M.p. about 200°.

**Soluble** 1 in 334 of water, 1 in 35 of boiling water, 1 in 13.5 of alcohol 90%, 1 in 10 of solution of potassium hydroxide, also soluble in organic solvents

**Antidotes.** Empty stomach by emetic or stomach tube. Give medicinal charcoal stirred up in water. For convulsions, give potassium bromide 2 dr. and chloral hydrate 20 gr, repeated if necessary. Keep patient lying down and warm. Stimulants

It is a powerful convulsive poison, differing from strychnine in that it acts mainly on the medulla. Gives good results in checking night-sweats (does not, like atropine, cause dryness of the throat), also employed in epilepsy and chronic alcoholism. Overdoses cause stupor, delirium and convulsions. It increases the secretion of the mucous and sweat glands. Its action in checking night sweats is explained by Cushny as probably due to its increasing the respiration and thus preventing that stimulation of the nervous mechanism of perspiration which occurs through the partial asphyxia. It may be given in pills, to be taken for 2 or 3 nights successively. The drug is slightly cumulative, and may thus be temporarily stopped with effects persisting. A pill of picrotoxin  $\frac{1}{10}$  gr, atropine  $\frac{1}{10}$  gr, with agaricin  $\frac{1}{2}$  gr., is said to act even better.

[P1 81] **Cocculus Indicus** (B.P.C.) *Syn.* LEVANT BERRIES

The fruit of *Anamirta paniculata* (Menispermaceæ), containing 1.0 to 1.5% of picrotoxin. Has been used as an ointment for pediculi (1 in 60) also as tincture (1 in 10) and liquid extract (1 in 1)

[P1 81] **Yohimba** (B.P.C.)

[P1] "*Alkaloids, the following; their salts, simple or complex — Yohimba, alkaloids of.*"

[81] "*Alkaloids, the following; their salts, simple or complex — Yohimba, alkaloids of.*"

[86] "*Alkaloids—Yohimba, alkaloids of—specify proportion as the proportion of any one alkaloid of yohimba that the preparation would be calculated to contain on the assumption that all the alkaloids of yohimba in the preparation were that alkaloid.*"

The bark of *Pausinystalia yohimba* (Rubiaceæ), containing 0.3 to 1.5% of alkaloids, chiefly yohimbine.

[P1-81] **Yohimbinae Hydrochloridum** (B.P.C., P.G. VI, P. Helv V).  $C_{21}H_{26}O_3N_2.HCl = 390.7$ .

*Dose.*— $\frac{1}{10}$  to  $\frac{1}{2}$  grain (0.003 to 0.008 g), in pills or by hypodermic injection.

White odourless crystalline powder with bitter taste. M. p. about 300°.

**Soluble** 1 in 100 of water, more soluble in hot water and in alcohol 90%.

**Uses.** Aphrodisiac, increasing the pelvic reflexes. A few drops of a solution  $\frac{1}{2}$  to 1% strength act as an anæsthetic when applied to the cornea.

[P1-81] **Yohimbina.** *Prop Name.* APHRODINE (C. Zimmermann, London). In white crystals soluble in organic solvents; m p. 234°.

[P1-81] **Juvenin** (Bayer Products, London) Yohimbine methylarsinate and strychnine methylarsinate. *Dose* —1 tablet (0.1 g) thrice daily or 1 ml subcutaneously every second day. For sexual neurasthenia.

[P1-81] **Menolysin** (Braun, London) Yohimbine hydrochloride in tablets (0.005 g) and ampoules for subcutaneous injection (0.05 g in 1 ml) In dysmenorrhœa and amenorrhœa. Also in compound tablets containing 0.005 mg with 0.03 g codeine phosphate

[P1-81] **Tonicamps** (Paines & Byrne, London). Ampoules of 1 ml containing strychnine and yohimbine monomethylarsenate. Asthenia and sexual impotence

[P1-81] **Yohidrol** (Riedel-de Haen, Berlin, Old Strand Chemical Co., London) Yohimbine hydrochloride tablets containing 0.005 g. *Dose* —Up to 6 tablets a day in sexual impotence

## SULPHONAL

B P



*Syn.* SULPHONMETHANUM (*Fr. Cx.*, *P.G. VI*, *P. Hung*, *P. Helv. V*, *P. Dan.*, *P. Belg. IV*, *F.E. VIII*), DIETHYLSULPHONEDIMETHYLMETHANE.

[P1] "Sulphonal, alkyl sulphonals"

[84] "Sulphonal, alkyl sulphonals."

*Dose* —5 to 20 grains (0.3 to 1.2 g), in cachets or suspended with mucilage. *P.G. VI* and *Fr. Cx. Supp.* 1920 have max. single dose 1 g., max. during 24 hours 2 g. (*F.E. VIII* 1 and 3 g. respectively) Should be finely powdered and followed by a draught of hot fluid. Unless in solution the dose should be given 1 to 2 hours or more before sleep is desired.

In colourless crystals or powder, tasteless and odourless. M p. about 126°.

**Soluble** about 1 in 450 of water, 1 in 15 of boiling water, 1 in 80 of alcohol 90%, freely in hot alcohol, 1 in 90 of ether, 1 in 3 of chloroform

**Antidotes.** Empty stomach by emetic or stomach tube. Keep patient lying down and warm, but keep him roused. Give sodium bicarbonate in dilute solution freely. Stimulants, e.g., hot strong coffee, strychnine  $\frac{1}{2}$  gr., or caffeine sodium benzoate 2 gr., hypodermically. Coramine, 5 to 15 ml. of 25% solution, intravenously. Dextrose intravenously. Artificial respiration and inhalations of oxygen with 7% carbon dioxide if necessary. Lumbar puncture and drainage, to remove the poison which has passed into the cerebrospinal fluid, may be required.

HÆMATOPORPHYRINURIA, followed by increasing weakness, flaccid paralysis and death, after lengthy treatment with sulphonal (20 gr. daily for 3 months).--Wilfred Harris, *Lancet*, ii/1922, 854.

**Uses.** Hypnotic, but is not curative of pain; does not affect digestion, pulse, or temperature and is especially desirable for

nervous subjects. Useful in chorea. 30 grains may be given in solution in 1 ounce of brandy with 2 ounces of boiling water added (= about 140°F.). Is slow in action on account of slight solubility. Excretion is very slow, hence it is cumulative. Frequent administration may produce hæmatoporphyrinuria and it should only be given occasionally.

[P1-84] **Haustus Sulphonal.** Sulphonal 20 gr, mucilage of acacia 2 dr., syrup 30 m., water to 1 oz.

[P1 84] **Tabellæ Sulphonalis** (B P C.). Contain 5 gr. (0.3 g.).

[P1-84] **Methylsulphonal** (B P., P. Ned. V, P.G. VI, F E. VIII).  $(\text{CH}_3)(\text{C}_2\text{H}_5)\text{C}(\text{SO}_2\cdot\text{C}_2\text{H}_5)_2 = 242.3$ . *Syn. and Prop Name.* DIETHYLSULPHONEMETHYLETHYLMETHANE, SULFONETHYLMETHANUM (U.S.P. XI), METHYLSULFONALUM (P Belg. IV, P Helv. V), TRIONAL (Bayer Products, London).

*Dose* —5 to 20 grains (0.3 to 1.2 g.), in cachets, in a large cup of hot liquid *Fr Cx Supp* 1920 gives latter approx as max. single, and during 24 hours. *P. Helv V* max. single dose 15 grains, max. during 24 hours 30 grains *U.S.P. XI* average dose 12 grains.

An oxidation product of mercaptol made by the condensation of methylethylketone with ethylmercaptan. In crystalline scales or microcrystalline powder, m. p. about 77°.

**Soluble** 1 in 320 of water, 1 in 12 of alcohol 90%, and in ether.

**Antidotes.** Treat as for poisoning by sulphonal, p. 871.

**Uses.** Has a stronger hypnotic action than that of sulphonal. Has cured chorea. Useful for the insane. Methylsulphonal is more effective in sleeplessness connected with neurasthenia and organic brain disease. Both are useless in insomnia due to pain, and in morphine and cocaine habits.

[P1 84] **Tabellæ Methylsulphonalis** (B P C.) contain 5 gr (0.3 g.)

## SULPHUR

S = 32.06.

**Sulphur Præcipitatum** (B.P., U.S.P. XI, P Dan.). *Syn.* MILK OF SULPHUR.

*Dose* —15 to 60 grains (1 to 4 g.), in milk or treacle, or as confection of sulphur with or without confection of senna. *U.S.P. XI* average dose 1 dr.

A soft powder free from grittiness, obtained by boiling sublimed sulphur with calcium hydroxide and water and decomposing the resulting solution with hydrochloric acid. Under a microscope it is seen to consist entirely of amorphous particles with no associated crystals. M.p. about 115°, forming a mobile liquid which darkens and becomes viscid on heating to 160°.

**Soluble** almost completely in carbon disulphide, also soluble in benzene, ether, chloroform, light petroleum and oil of turpentine.

**Uses.** Internally it has no action on the stomach but a certain proportion administered is converted into alkali sulphides in the intestines with consequent mild laxative effect. Given internally it has been employed for skin affections, occasionally benefiting chronic eczema with much itching. Hale White says its powers in arthritic affections are doubtful. Externally, sulphur is commonly used to cure scabies and for acne.

Sweating of the feet has been treated by drachm doses thrice daily.

As an antiseptic, sulphur 25% *w/w* suspended in glycerin has been injected into suppurating sinuses.

**SEBORRHOIC ALOPECIA** treated by saturated solution of sulphur in carbon disulphide—Sabouraud, *Brit. med. J.*, 11/1925, 984

**Balneum Sulphuris (B.P.C.)** Contains freshly precipitated sulphur obtained from 5 oz. each of sodium thiosulphate and sodium acid sulphate per 30 gallons

**Confectio Sulphuris (B.P.)**

**Dose.**—1 to 2 drachms (4 to 8 g)

Contains 45% of precipitated sulphur with 11% of potassium acid tartrate, tragacanth, syrup, glycerin and tincture of orange.

**Lotio Sulphuris (B.P.C.)**

Precipitated sulphur 30 gr. in glycerin, alcohol, rose water and solution of calcium hydroxide to 1 oz

**Lotio Sulphuris (C.X.H.)**

Precipitated sulphur 20 gr, glycerin 10 m, industrial methylated spirit 15 m, lime water 2 dr, water to 1 oz

**Lotio Sulphuris Composita (C.X.H.)**

Precipitated sulphur 15 gr, zinc sulphate 15 gr, sulphurated potash 15 gr, water to 1 oz

**Lot. Sulphur Co. (N.I.F.)** Precipitated sulphur 2 dr, glycerin 80 m, industrial methylated spirit  $\frac{1}{2}$  oz, solution of calcium hydroxide to 8 oz.

**Lotio Sulphuris cum Sapone.**

Precipitated sulphur 30, Cologne spirit 60, glycerin 4, soft soap  $\frac{1}{2}$ , rose water to 500 For acne of the face

**Trochisci Sulphuris (B.P.C.)**

**Dose.**—1 to 6.

Contain precipitated sulphur 5 gr. and potassium acid tartrate 1 gr. For skin and rheumatic affections

Garrod's formula is 4 grains of precipitated sulphur with 1 gr. of potassium acid tartrate

**Unguentum Sulfuris (U.S.P. XI)**

Precipitated sulphur 15, wool fat 5, yellow wax 5, white petrolatum 75.

**Azudine (Lilly, London).** Precipitated sulphur 10%, phenol 1%, with camphor, menthol and balsam of Peru in an ointment base

**Sulphur Sublimatum (B.P., U.S.P. XI, P. Dan.).** *Syn.* FLOWERS OF SULPHUR.

A slightly gritty powder. Under a microscope is seen to consist chiefly of rounded amorphous particles or aggregates occasionally associated with semi-crystalline masses

**Soluble** almost completely in carbon disulphide, about 1 in 4 of petrol, benzene or toluene, about 1 in 70 of chloroform, 1 in

125 of almond oil, 1 in 200 of olive oil or cotton-seed oil, 1 in 70 of sesame oil. Insoluble in water or alcohol 90%.

**Uses.** Is used for the same purposes as precipitated sulphur, especially in ointments for skin affections and for scabies. A solution of sulphur in oil administered by intramuscular injection is used for the production of artificial pyrexia in the treatment of general paralysis of the insane, various forms of arthritis and in dementia præcox (*see* Oleum Sulfuris below) A 1% aqueous suspension is also sometimes used

**Sulphur Lotum** (*U.S.P. XI, P. Helv. V*) is sublimed sulphur washed with ammoniated water.

**Sulphur Nigrum** was the name formerly applied to native Sicilian sulphur. It is now applied to the residuum from the subliming pots, or to sublimed sulphur mixed with charcoal. Is used in veterinary medicine.

**Unguentum Picis et Sulphuris** (*L.H.*) *Syn* WILKINSON'S OINTMENT  
Sublimed sulphur 2 dr, tar 2 dr, potash soap 4 dr, benzoinated lard 4 dr, purified talc 1 dr.

#### **Unguentum Sulphuris** (*B.P.*)

Sublimed sulphur 10% in yellow simple ointment.

Scabies is treated by sulphur ointment after washing with soft soap. Use equal parts of the *B.P.* ointment and soft paraffin.

#### **Unguentum Sulphuris Camphoratum** (*B.P.C.*)

Sulphur 2% with phenol, resorcinol, camphor and solution of coal tar in lard and white soft paraffin.

#### **Unguentum Sulphuris Compositum** (*B.P.C.*)

Sublimed sulphur 15%, tar 15% and calcium carbonate 10%, in lard and soft soap.

#### **[P] Unguentum Sulphuris cum Hydrargyro** (*U.C.H.*)

Sublimed sulphur 30, sublimed mercuric sulphide 2, ammoniated mercury 2, arachis oil 12, lard 54. Useful in skin diseases

#### **Unguentum Sulphuris et Betanaphtholis Salicylatum.**

Sulphur  $\frac{1}{2}$  dr, salicylic acid 10 gr, betanaphthol 3 gr, yellow soft paraffin 1 oz. Tinea circinata can be rapidly cured with this ointment.

**Unguentum Sulphuris et Resorcinolis** (*B.P.C.*). Sulphur 4.5% and resorcinol 3% in yellow soft paraffin.

**Unguentum Sulphuris et Zinci cum Kaolino.** Sulphur 4, zinc oxide 3, kaolin 1, benzoinated lard 8. For sweating of the feet.

#### **Oleum Sulphuris.**

**Dose.**—0.5 ml. increased up to 10 ml. To be given on alternate days intramuscularly—supraperiosteally on the lateral surface of the femur.

A 1% solution of sulphur in olive oil. The injections set up a febrile condition of short duration. The dose should be increased by 0.5 ml. on each occasion until the desired temperature is reached. The aim is to reach 104°F gradually. Usually 5 ml. is the maximum dose required.

**CHRONIC NON-SPECIFIC ARTHRITIS** Treatment of 50 cases by intramuscular injection of Sulfosin, starting with 0.5 ml., after which further injections are given every 5 or 6 days in steadily increasing amounts up to (usually) 4 or 5 ml

After the third dose, massage, passive movement, and some form of heat therapy found useful between injections. Results show that considerable improvement may be expected in a proportion of patients in whom the changes are limited to the soft structures about the joint and are not permanent in nature, but less improvement when damage of a permanent kind is present. Treatment should not be given during the acute phase in elderly, feeble, emaciated, nervous or very obese patients, or in patients with active organic disease other than arthritis.—D. Krestin, *Brit. med. J.*, 11/1935, 1144.

**DEMENTIA PRÆCOX** treated, starting with 1 ml. and increasing by 1 ml. up to 12 injections. Sweating, loss of appetite, leucocytosis, and rise of temperature. Progressive dementia may be prevented.—P. C. Collingwood Fenwick, *Lancet*, 1/1931, 241.

**G.P.I.** High fever produced. Treatment of G.P.I. worth trial.—N. G. Harris, *Lancet*, 1/1930, 1069. Good pyrexial reactions.—W. H. Shilcock, *Lancet*, 11/1930, 347.

Consecutive temperatures of 104° or 105° F, as in induced malaria, not obtained with Sulfosin.—W. G. Patterson and S. R. L. Switzer, *Lancet*, 11/1930, 348.

Painful and useless. A number of other methods—"experiments"—ineffective in Vienna.—*Lancet*, 1/1930, 375.

High temperature within 24 hours. Produces considerable leucocytosis.—T. D. Power, *Lancet*, 11/1930, 1289.

Suitable for advanced cases of G.P.I., because harmless, especially on a degenerate myocardium. Results compare favourably with malarial pyrexia.—J. H. R. Laptain, *Lancet*, 1/1931, 635.

Where malarial treatment fails in G.P.I., or cannot be used, sulphur produces an excellent pyrexia, a suspension in olive oil producing the most constant reaction and leucocytosis.—N. G. Harris and J. A. B. Hicks, *Lancet*, 11/1932, 387.

Repeated injections may have therapeutic effect in general paralysis, neurosyphilis, and other syphilitic—and certain non-syphilitic—lesions of the central nervous system. Better than malarial infection treatment.—K. Schroeder, *Lancet*, 11/1929, 1081, 11/1930, 549.

**SCHIZOPHRENIA.** In no way a specific in the treatment of the psychoses, but merits a trial in early cases of schizophrenia not responding to occupational therapy. Patients not benefiting from first course fail to respond to subsequent courses.—P. K. McCowan and M. L. M. Northcote, *Lancet*, 11/1932, 238.

**Colsul** (Crookes Laboratories, London) 1% solution of sulphur in vegetable oil, also a 1% aqueous colloidal suspension. *Dose*.— $\frac{1}{2}$  ml. initially increased at each injection by  $\frac{1}{2}$  ml. to a maximum of 5 ml. or until a sufficient degree of pyrexia is obtained (10 to 12 ml. have been used).

**Sulfosin** (Leo, Copenhagen, Bencard, London). Solution of sulphur in oil for artificial fever therapy.

**Sulphur Sterules** (Martindale, London) contain 1 ml. of 0.1% solution in poppy-seed oil or 1 to 10 ml. of 1% solution in oil.

**Sulphuris Chloridum (B.P.C.).** *Syn.* SULPHUR MONOCHLORIDE  $S_2Cl_2 = 135.0$ .

A reddish-yellow mobile fuming liquid with disagreeable penetrating odour. Decomposed by water or moist air, giving sulphur and hydrochloric and sulphurous acids.

**Unguentum Sulphuris Hypochloritis (B.P.C.).**

Sublimed sulphur 12% and sulphur chloride 2%, with oil of bitter almonds (s.A.P.), in lard. For scabies.

**Sulphuris Iodidum (B.P.C.).** *Syn.* SULPHUR SUBIODIDE.

A greyish-black crystalline solid containing not less than 70% of I.

**Unguentum Sulphuris Iodidi (B.P.C.).** Sulphur iodide 4% in glycerin and simple ointment. Used in acne rosacea, tinea and other parasitic skin diseases.



**Contramine** (*British Drug Houses, London*). Diethyl-ammonium-di-ethyl-dithio-carbamate,  $\text{SNH}_2(\text{C}_2\text{H}_5)_2\text{CSN}(\text{C}_2\text{H}_5)_2 = 222.3$ .

Occurs as white crystals, soluble 1 in  $2\frac{1}{2}$  of water, and available in ampoules of sterile solution for intramuscular injection. It is used in the chronic complications of gonorrhœa, including stricture, chronic epididymitis, conjunctivitis and iritis, and varied forms of chronic rheumatism.

**Dose.**—Intramuscularly  $\frac{1}{2}$  grain (0.05 g.) to 4 grains (0.25 g.) in 1 to 2 ml. of cold sterilised water or saline. Must not be heated.

The usual initial dose (intramuscularly) is 0.125 g. in 1 ml.

**Contramine Pessaries** are prepared for use in chronic cervicitis and endometritis. Bougies and suppositories are also made.

Local application of Contramine solution may assist healing of chronic ulcers. In cases of sinuses in muscles, closure is often obtained by intramuscular injections around the lesion.

In severe cases of metal intoxication 0.125 g. may be injected intramuscularly every day till 6 or more doses have been given. In other cases 2 injections of 0.125 g. with a week's interval usually suffice.

**Mitigal** (*Bayer Products, London*). Dimethyl-diphenylene-disulphide. Liquid organic sulphur preparation for treatment of skin diseases by local application.

**SCABIES.** Cured by one application after having tried Ung. Sulph. *ad nauseam*.—T. L. Hillier, *Brit. med. J.*, i/1933, 128. See also M. Newman, *ibid.*, and R. D. Moyle, *ibid.*, 172; also A. D. Matthews, *ibid.*, i/1934, 16.

### Colloidal Sulphur.

**Manufacture.** A 1 in 1000 opalescent colloidal sulphur solution is made by decomposition of a mixture of sodium sulphide and sodium sulphite with acid in the presence of protective colloid.

For use in skin affections and wherever sulphur is indicated through excessive elimination.

**Colloidal Sulphur B.R.I.** (*British Drug Houses, London*). A colloidal sulphur complex for administration by intramuscular or intravenous injection in the treatment of arthritis.

**Collosol Sulphur** (1%) (*British Colloids, London*). A colloidal solution of sulphur. **Dose.**—*Per os* 2 to 4 drachms (8 to 15 ml.) in a wineglass of water twice daily during or after principal meals. Subcutaneously or intravenously 1 to 2 ml. In rheumatic and skin affections.

**Sarcopitol** (*Anglo-French Drug Co., London*). Colloidal sulphur compound for local application in seborrhœa, scabies, eczema, alopecia, etc.

### Sulphuretted Hydrogen Poisoning.

Encountered in industries such as artificial silk works, chemical works, sewage works, etc.; it is stated that the maximum safe concentration for 6 hours may be taken as 1 in 20,000, but to avoid eye irritation and general lowering of health, it is advisable to keep it well below this.

Prolonged inhalation of sulphuretted hydrogen, even in as low a concentration as 100 parts per million, is reputed to induce symptoms of chronic intoxication. Strictly speaking, it is an irritant gas.—*J. Amer. med. Ass.*, ii/1925, 119, see also L. W. Smith and co-workers, *ibid.*, 177.

**Antidotes.** Place patient in fresh air, apply artificial respiration and keep it up steadily. Inhalations of oxygen with 7% carbon dioxide. Give stimulants carefully; coffee by rectum if patient cannot swallow. Iodised starch (5% iodine rubbed into starch with a little water and dried) has been suggested. Inhalation of chlorine recommended.

**Selenium** (Se = 79.2) and **Tellurium** (Te = 127.5). Selenium and tellurium belong to the sulphur group. Selenates and tellurates are highly poisonous—unlike sulphates.

**Colloidal Selenium.**

Colloidal solutions of selenium have been advocated in the treatment of inoperable cancer.

For a full description of the selenide treatment of cancer, see A. T. Todd, *Brit. J. Surg.*, 1934, 619. See also A. T. Todd, *Med. Pr.*, Oct. 21, 1936 (supplement).

**Radio-Active Selenide** (*British Drug Houses, London*). *Syn.* R.A.S. A feebly radio-active preparation, made by combining certain radium residues with selenium, for use in the treatment of cancer by the Bristol Royal Infirmary methods.

**Colloid Sulphur-Selenium.** *Syn.* SSs. A double colloid of sulphur and selenium for use in conjunction with R.A.S.

Intravenous injections daily for 10 days of 5 to 10 ml. of a 1 in 2000 isotonic solution definitely and undoubtedly ameliorates patient's condition and prolongs life in many cases of gastric cancer. Absolutely safe and no contraindications. Repeat treatment after interval of 10 days or a fortnight. Three courses may be given in 3 months, and possibly more, depending on progress of patient—Stanley Wyard, *Diseases of the Stomach*, p. 358.

Malignant disease treated by selenium. Large doses (5 ml.) "spell disaster." Temporary improvement only can be expected.—A. S. Gillett and C. P. G. Wakeley, *Lancet*, i/1922, 804; *Brit. med. J. Ept*, ii/1922, 15.

The report of an investigation by the Medical Committee of the Royal Cancer Hospital on the treatment of 70 cases of cancer between October, 1934, and August, 1935, with colloidal selenium. Of the 70 cases treated, 41 have died, 21 are still under treatment, 7 have refused further treatment, and 1 who received merely prophylactic treatment is still without evidence of recurrence. Of the 41 cases which died, in 37 the treatment appeared to have no effect whatever, and in 4 there was transient alleviation of pain. Of the 21 cases still alive, in 3 the growth appears stationary, in 2 there was temporary diminution not maintained, in 10 there was definite alleviation of pain and improvement of the general condition, and in 6 the period of observation was too short for results to be shown—*Lancet*, i/1936, 1198.

The dosages of colloid were far too low, and chemical alteration occurred during injection, the X-ray dosage was standardised, and, with the low dosage of colloid, must have been almost inoperative. A comparison of the method described with the original should have shown such discrepancies that to call it an independent test is far from the truth.—A. T. Todd, *Lancet*, i/1936, 1262.

**Tellurium in Syphilis.** Experiments on rabbits showed that apparently tellurium injected becomes soluble by combining with tissue protein. Tellurium metal, the oxide,  $\text{TeO}_2$ , and the iodoquinone, have been used clinically by Fournier and others with disappearance of spirochaetes. 5 ml. of 5% tellurium suspension intramuscularly in  $\frac{1}{2}$  to 1 ml. doses at intervals of 5 to 7 days. Toxicity appears to be slight. Methyl telluride excreted with strong smell of garlic a disadvantage, persisting 6 to 8 months. Loss of hair pigment observed. Tried in Wassermann-fast cases with apparent success.—A. D. Frazer, *Lancet*, ii/1930, 133, see also C. Levaditi, *Brit. med. J.*, ii/1928, 537.

**Colloidal Tellurium, B.R.I.** (*British Drug Houses, London*). A colloidal preparation of tellurium for administration by injection in the treatment of chronic rheumatism.

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## SUPPOSITORIA

Suppositories are medicated masses intended for anal administration. They are usually conical at one end, the other end being flat so that the suppository is retained more easily by the sphincter muscle after insertion. It is customary to employ moulds which hold 1 g. (15 gr.) or 2 g. (30 gr.) of oil of theobroma. Unless otherwise specified, the 15-gr. size is supplied.

The bases employed for suppositories are oil of theobroma, glycerin suppository mass and occasionally freshly prepared soap

as in glycerin soap suppositories. It is essential that the melting-point of any suppository mass shall be between  $30^{\circ}$  and  $35^{\circ}$ . Oil of theobroma is usually employed unless the prescriber otherwise directs, and when the suppositories are prepared by melting and moulding, care should be taken not to overheat this base since, as with many other substances, overheating will cause a lowering of the solidifying-point and subsequent difficulty in setting. Because of this it is preferable to use powdered or shredded oil of theobroma. Certain medicaments such as phenol, chloral hydrate and resorcinol cause an appreciable lowering of the melting-point of oil of theobroma when warmed with it. In preparing such suppositories, the melting-point may be brought back to normal by incorporating a little white wax. This addition may be avoided, except in the case of suppositories containing volatile oils, by using the minimum amount of heat.

Glycerin suppository mass has a limited use as a base because its gelatin content renders it incompatible with certain medicaments, particularly tannins. Ichthammol will occasionally form a water-insoluble mass which does not melt below body temperature. A 1-g. (15-gr.) mould will hold 1.2 g. (18 gr.) of glycerin suppository mass. If the large proportion of glycerin present in the mass is not desired, the following basis is a good substitute: Gelatin 10 g., water 40 ml.; soak, dissolve with gentle heat, add glycerin 15 g., and evaporate on a water-bath until the mass weighs 25 g.

#### ***Suppository Mass for Hot Climates.***

Oil of theobroma is generally used, and it is customary to incorporate varying quantities of white wax according to the prevailing temperatures. 5 to 15% is commonly employed. Different samples of both oil of theobroma and white wax may each have different melting-points, so that variation will occur in mixtures. Using an oil of theobroma with m.p.  $33.89^{\circ}$  and white wax with m.p.  $61^{\circ}$ , the melting-points of mixtures are as follows:—

<i>% White Wax</i>	<i>Melting Point.</i>
2½	32 6°
4.5	33 06°
10	39 44°
15	46 11°
20	50 00°

Suppositories should be sent out in partitioned boxes lined with waxed paper, and, when made with glycerin suppository mass, they should be slightly greased with oil. When they contain volatile and hygroscopic ingredients, or when intended for export to tropical climates, they should be wrapped separately in tinfoil.

**Pessl.** Pessaries are medicated masses intended for insertion into the vagina. They may be made with a basis of oil of theobroma or glycerin suppository mass. If the basis is not specified, it is usual to use oil of theobroma. Pessaries produce a continued

action on the parts in leucorrhœa, also for ulceration and inflammation of the cervix uteri. They are usually prepared like suppositories by moulding, the mould having an oil of theobroma capacity of 8 g. (120 gr.) The shape may be convex or suppository-shaped.

To be efficient, pessaries must be inserted as far as possible whilst the patient is in the supine position with the hips raised. They are most effectual at bedtime

***Pessary Mass for Hot Climates.***

Mixtures of white wax and oil of theobroma are usually used (*see* suppositories, p. 877).

**Tampons.** Consist of plugs of non-absorbent cotton-wool, globular in shape, about  $1\frac{1}{2}$  in in diameter, and covered with gauze. They are medicated by saturating them in a solution of the medicament, the usual solvent being glycerin

**Glycerin Tampons.** Saturated with glycerin **Mild Silver Proteinate Tampons,** containing 1, 5 and 10% mild silver proteinate in glycerin. **Ichthammol Tampons** saturated with 5, 10 or 20% ichthammol in glycerin **Iodoform Tampons,** with 5% iodoform in glycerin

**Pontampons** (*Pontampon Co., London*) consist of a semi-solid slowly-soluble medicated cone with a non-absorbent wool tampon attached, the whole encased in a soluble gelatin shell

For the treatment of gonorrhœa, endometritis, cervicitis, vaginitis, leucorrhœa, dysmenorrhœa, prolapsus uteri Numerous medicated products are available

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## TABELLÆ

### COMPRESSED TABLETS

Tablets of medicaments are usually preferable to pills, since less excipient is required and the risk of not disintegrating in the alimentary tract is lessened. They may be of several types.

(a) **Easily friable and readily disintegrated after swallowing,** for such substances as acetylsalicylic acid, phenazone, phenacetin. This is obtained by using the minimum amount of compression and incorporating from 5 to 15% of potato starch.

(b) **Hard Tablets** which slowly disintegrate or dissolve. These are obtained by using heavy compression which produces a tablet resembling a lozenge. Substances such as potassium chlorate or bromide, and ammonium chloride are made into tablets of this type. They are intended either to be dissolved slowly in the mouth or to be dissolved in water and taken as a draught.

(c) **Solvellæ,** or solution-tablets, which are intended to be dissolved in water for external or local use. When they contain poisonous ingredients a suitable dye is often added to distinguish them.

(d) **Tablet-triturations.** These are small tablets made with the minimum of compression in special metal or vulcanite moulds

and intended to be crushed to powder before use. They consist of substances such as mercury with chalk, calomel, etc., which are usually prescribed as powders.

(e) **Hypodermic Tablets.** These are very small tablets, machine-made, readily soluble in water, and used for the preparation of subcutaneous injections. They contain a basis of sterilised lactose, and are made and packed under controlled aseptic conditions.

**Preparation of Tablets.** Fine powders will not compress to tablets, and it is necessary to convert such material into granules. If, however, the medicament is in the form of small crystals no further preparation is necessary. Thus, such substances as potassium bromide, chlorate or permanganate, sodium chloride, heavy crystal forms of acetylsalicylic acid, phenacetin, and phenazone only require drying and passing through a No. 16 sieve and any loose powder shaking out on a No. 30 sieve. The material can then be fed directly into the machine or, if a friable tablet be required, mixed with 5 to 15% of potato starch, and then compressed.

In the preparation of granules, it is necessary to add some liquid which will damp the mass so that it will cohere in small lumps on passing through a No. 16 sieve and remain as hard granules on drying. The liquid used will vary with the medicament. A little alcohol is suitable for material which contains alcohol-soluble constituents, for example alcoholic extracts such as the dry extracts of belladonna and hyoscyamus.

By the use of vacuum drying it is possible to produce a dry mass in a very porous condition, so that on passing through a No. 16 sieve, granules quite suitable for immediate use in the tablet machine are obtained. Dry extract of cascara may be made suitable for tablet granules in this manner. The method could probably be extended to other similar extractives.

A general excipient which will be efficient in the majority of cases is a mixture of equal parts of syrup and dilute (1 in 4) mucilage of acacia. This is thoroughly worked into the powdered medicament until sufficient is present to give coherence on passing. It is then passed through a No. 16 sieve and dried at a temperature of about 40° in a drying oven. The mass is then resieved through the No. 16 sieve and loose powder shaken out on a No. 30 sieve. It is often advisable to include a little starch in the powder before granulation in order to ensure disintegration on swallowing.

In order to prevent sticking in the machine and to give an easy flow, from 1 to 3% of finely powdered French chalk may be added to the dry granules, as a lubricant, by shaking. Other lubricants may be used. Thus for tablets intended for the preparation of aqueous solutions, boric acid may be substituted. Liquid paraffin sprayed on to the granules is also used, and an emulsion of oil of theobroma has been recommended, but the oil of theobroma goes rancid on storage.

It is important that granules shall be of even size, free from much loose powder and thoroughly dry. Much of the trouble in tablet making results from neglecting the latter precaution.

In using the tablet machine, whether hand or power-driven, it is advisable to keep the punches in good condition. They should be kept well polished, if possible by "buffing" them on a polishing machine. An ordinary cork spiked on to the axis of the polishing machine and used with a trace of very fine emery powder forms a very suitable "buffing" surface. This precaution will tend to prevent "capping" or the splitting off of the surface of the tablet.

Owing to the necessity of granulating, tablets are rarely the same weight as the medicament. Thus a 5-grain tablet usually weighs from 5½ to 6½ gr.

**Tablet-triturates.** The mould consists of two plates, one with perforations and another with pegs corresponding in size and position with the perforations. If the medicament has a small dose, such as calomel or strychnine hydrochloride, it is necessary to make a dilution with lactose to give bulk. The powder is then dampened with 60% alcohol to give coherence and passed into the perforations. A spatula is used to ensure complete filling of each cavity and to smooth off excess. The filled plate is superposed on the pegs and pressed down, leaving damp tablets on the latter. The tablets are then dried. In order to ascertain the capacity of the mould, a few trial tablets must be made. Moulds

are made in a range of sizes  $\frac{1}{2}$  to 4 grains, and will prepare 50 to 250 tablets at one time.

Notes on the manufacture of tablets.—*Pharm J.*, 11/1908, 276; *ibid*, 11/1911, 432; *ibid*, 11/1935, 475, 503.

## THEOBROMATIS SEMEN

(with THEOBROMINE and THEOPHYLLINE)

B.P.C.

Syn. CACAO OR COCOA SEED.

The seeds of *Theobroma Cacao* (Sterculiaceæ) containing in the kernel about 1 to 3% of theobromine, a small amount of caffeine and 40 to 60% of fat. The shell contains about  $\frac{1}{2}$  to 2% of theobromine. When heated and deprived of husk and membrane, these yield cocoa nibs. The nibs with most of the oil pressed out produce, when reduced to powder, cocoa for use as a beverage. Before expression of fat the seeds may be treated with an alkali, and flavouring such as vanillin may also be added.

It is improbable that either vitamin D or ergosterol is present in the fresh shell of the cacao bean. During fermentation, yeast, containing ergosterol, develops in the pulp on the shell. During drying in the tropical sun the ergosterol is converted into vitamin D. Hence the order of vitamin D potency of the shell of the cacao bean is (1) artificially dried—absent; (2) not deliberately fermented but slightly fermented during sun-drying—fairly high, approaching the potency of dairy butter, (3) fermented and sun-dried—very high, 20 or 30 times the potency of dairy butter—A. W. Knapp and K. H. Coward, *Biochem J.*, 1935, 2735.

**Oleum Theobromatis** (B.P., U.S.P. XI, P. Helv. V) Syn. CACAO BUTTER, COCOA BUTTER, CACAO OLEUM (P. Belg. IV).

The concrete oil of the seeds (yield about 45%). M.p. about 30° to 35°, i.e., below the temperature of the body. It is therefore much used for suppositories. For substances which lower the melting-point of the oil, and for export to hot climates, it is well to add 5 to 15% of white wax. (See Suppositoria.)

**Soluble** freely in ether, chloroform and light petroleum, slightly soluble in alcohol 90%.

To deodorise for cooking, heating the oil in an open pan to 188° for 5 minutes has been suggested, and, to give it the consistence of butter, adding 5 parts of cotton-seed oil to each 4 parts of cacao butter has been recommended.

**Pasta Theobromatis.** Syn. CHOCOLATE

This is made by grinding the nibs into a paste, with sugar and vanilla or other flavouring added; it contains about 40 to 60% of sugar and about 28 to 38% of fat.

**Theobromina** (B.P.C., P. Helv. V, P. Dan., P. Ned. V) Syn. 3 : 7-DIMETHYLXANTHINE, SANTHOSE.

$C_7H_8(CH_3)_2O_2N_4 = 180.1$ .

**Dose.**—5 to 10 grains (0.3 to 0.6 g.).

A white, crystalline, neutral powder with bitter taste.

**Soluble** 1 in 1000 of water, 1 in 115 of boiling water, 1 in 1400 of alcohol 90%; sparingly soluble in ether.

2% aqueous solutions may be obtained with aid of trisodium phosphate.

**Uses.** As a diuretic, relieves cardiac and renal dropsy by increasing permeability of the kidneys, especially in conjunction with digitalis. In angina pectoris, 20 to 30 gr. doses spread over 24 hours lessen the frequency and severity of attacks

Has elective action on elimination of chlorides, and increase of urinary chlorides follows. Some hold it should be limited to nephritis with œdema, accompanied by chloride retention. In other forms may be harmful — *Brit med. J. Epit.*, 1/1930, 74.

**Theobromine Calcium Salicylate.** *Syn. and Prop. Names* THEOCALCINE, CALCIUM-DIURETIN (*Knoll, Ludwigshafen; Pharmaceutical Products, London*), CALCOTHEOBROMINE (*Richter, London*).

**Dose.**—7 to 15 grains (0.5 to 1 g.) Tablets, 7½ grains (0.5 g.) each.

A white powder slightly soluble in water, containing about 48% of theobromine and 11% of calcium. Prepared similarly to the sodium salt from theobromine, calcium oxide and calcium salicylate.

**Uses.** Similar to theobromine sodium salicylate. For arteriosclerosis 30 grains have been given daily, and up to 75 grains daily to achieve diuretic effect

**ASTHMA** Calcium-Diuretin taken once or twice in the evening stated to be an almost certain preventive — *Brit med. J. Epit.*, 1/1926, 16

**Raminal** (*Napp, London*) Tablets containing theobromine calcium salicylate 1½ gr., chlorophyll ½ gr., iron phosphate ½ gr. **Dose**—2 tablets thrice daily. Hypertension, angina pectoris, arteriosclerosis, cardiac asthma

[**P1 81**] **Vasobroman** (*Richter, London*) Tablets containing theobromine calcium salicylate 0.25 g., papaverine hydrochloride 0.01 g., bromoisovaleryl-carbamide 0.2 g. **Dose**—1 or 2 tablets thrice daily. Arteriosclerosis and hyperpiesis.

**Iod-Calcium-Diuretin** (*Knoll, Ludwigshafen, Pharmaceutical Products, London*). Tablets containing 7½ gr. of Calcium-Diuretin and 1½ gr. of potassium iodide. **Dose**—1 thrice daily after food; may be increased temporarily to 2 tablets thrice daily. As improvement sets in, the smaller dose should be resorted to and may be maintained for lengthy periods. In hypertonia, angina pectoris and asthma.

**Iodcalcotheobromine** (*Richter, London*) Theobromine calcium salicylate 0.25 g., potassium iodide 0.05 g. **Dose**—3 tablets daily. Arteriosclerosis, hypertension, etc.

**Rhoda-Calcium-Diuretin** (*Knoll, Ludwigshafen; Pharmaceutical Products, London*). Tablets containing 7½ gr. of Calcium-Diuretin and 1½ gr. of potassium thiocyanate. **Dose**—1 tablet thrice daily after food, 2nd and 3rd weeks, 1 tablet twice daily; 4th, 5th and 6th weeks, 1 tablet once daily. Crush in a little water or milk before swallowing. For treatment of hypertonia of climacteric or sclerotic origin, and in renal cases

**Theobromina et Sodii Acetas.** *Prop. Name.* AGURIN (*Bayer Products, London*).

**Dose.**—10 to 15 grains (0.6 to 1 g.), up to 45 grains daily in fresh solution.

White, crystalline, hygroscopic powder consisting of a mixture of sodium acetate with the sodium derivative of theobromine. Soluble 1 in 2 of water and about 1 in 200 of alcohol 90%.

In dropsy, sciatica and neurasthenia. Is strongly diuretic in action. Not to be given with acid substances, nor with sugar or

gum, and in general incompatible as for theobromine and sodium salicylate. To be preserved from the air, the  $\text{CO}_2$  of which tends to decompose it.

**Theobromina et Sodii Salicylas** (*B.P.*, *U.S.P. XI*, *P. Helv. V*, *P. Dan.*, *P. Ital. V*, *P. Belg. IV*, *P. Ned. V*, *P. Austr.*, *F.E. VIII*). *Prop. Name.* DIURETIN (*Knoll, Ludwigshafen; Pharmaceutical Products, London*).

*Dose.*—10 to 20 grains (0.6 to 1.2 g.). *P. Helv. V* has max. in 24 hours 90 grains approx.

**Manufacture.** Rub theobromine 18 to a paste with water 10. Dissolve sodium hydroxide 4 or *q.s.* in water 8 and add to the theobromine until clear. Add sodium salicylate 16, filter and evaporate on a water-bath or *in vacuo*.

A mixture of sodium theobromine ( $\text{C}_7\text{H}_7\text{NaO}_2\text{N}_4$ ) and sodium salicylate ( $\text{C}_7\text{H}_5\text{O}_3\text{Na}$ ) in approximately molecular proportions, containing not less than 46% of theobromine and not less than 41% of sodium salicylate. *U.S.P. XI* requires not less than 46.5% of the theobromine and not less than 35% of salicylic acid.

It is rapidly decomposed in moist air with absorption of  $\text{CO}_2$  and liberation of theobromine—hence less soluble in water. It must be kept in stoppered bottles.

**Soluble** 1 in 1 of water; insoluble in alcohol 90%, chloroform and ether.

**Incompatible** with ammonium salts, sodium bicarbonate and all acid salts, alkaloidal salts, free inorganic and organic acids, and aromatic spirit of ammonia.

**Uses.** Diuretic (*cf.* theobromine) without affecting nervous system and causing sleeplessness. Has prolonged effect when given with digitalis. Safe for scarlatinal diopsis of children. In angina pectoris it lessens the frequency of attacks.

**ANGINA PECTORIS** Purine-base diuretics are of value, but little to choose between any of the theobromine preparations. To avoid tolerance over a long period, the following (or some of them) were used on alternate weeks—Theobromine 5 gr., theobromine sodium acetate 10 gr., theobromine sodium salicylate 10 gr., theobromine calcium salicylate  $7\frac{1}{2}$  to 10 gr., theophylline 2 gr., theophylline sodium acetate 4 gr., theophylline-ethylenediamine  $1\frac{1}{2}$  to 3 gr. Four doses daily usually given (often best taken in the middle of a meal) for the first 4 days of each week. Will not give complete relief, but more helpful than any other drugs used.—N. C. Gilbert and J. A. Kerr, *J. Amer. med. Ass.* i/1929, 202.

**Tabellæ Theobrominæ et Sodii Salicylatis** (*B.P. C.*) contain  $7\frac{1}{2}$  gr. (0.5 g.).

**Theacylon** (*Merck, Darmstadt, Martindale, London*). Acetylsalicyloyl-theobromine

**Theophyllina** (*B.P. Add.*, *U.S.P. XI*, *P. Helv. V*, *P. Dan.*).  $\text{C}_7\text{H}_8(\text{CH}_3)_2\text{O}_2\text{N}_4\cdot\text{H}_2\text{O} = 198.1$ . *Syn.* 1:3-DIMETHYLXANTHINE.

*Dose.*—1 to  $2\frac{1}{2}$  grains (0.06 to 0.15 g.). No dose is given in *B.P. Add.*

White crystalline powder obtained from tea, or prepared synthetically. *M.p.*  $269^\circ$  to  $272^\circ$ .

**Soluble** 1 in 160 of water, 1 in 120 of water at  $25^\circ$ , 1 in 100 of alcohol 90%, 1 in 80 of alcohol 95% at  $25^\circ$ . Readily soluble



in alkali hydroxide solutions. Sparingly soluble in ether.

More strongly diuretic than theobromine, and also more irritant to the stomach.

The most effective of the xanthine diuretics. Best given in two doses of 0.3 to 0.5 g. with half a glass of water at 7 and 10 a.m.—H. A. Christian, *New Engl. J. Med.*, 1/1936, 419.

The addition of Theocin to digitalis therapy in dropsy often "tips the balance" and makes the kidneys act. Has proved suitable when both heart and kidneys diseased. The action is often very striking—within an hour. If no effect is manifested within 24 hours, or after 40 grains, it is of little use continuing the drug.—G. A. Sutherland, *Lancet*, 1/1917, 441.

**Deriphyllin** (*Homburg Pharma, London*). 1. 3-dimethylxanthine in combination with an oxyamine. Dose—0.5 to 2 ml. intravenously or intramuscularly; per os 20 drops to ward off attack, or 10 to 20 drops 3 times daily as prophylactic. Diuretic and vasodilator for œdema of cardiac and renal origin, cardiac asthma and angina pectoris.

**Theamin** (*Lilly, London*). Theophylline ethanolamine. Capsules contain 3 grains.

### **Theophyllina et Sodii Acetas** (*B.P., U.S.P. XI, P. Helv. V*)

**Prop. Name.** THEOCIN SODIUM ACETATE (*Bayer Products, London*).

**Dose.**—2 to 5 grains (0.12 to 0.3 g.) dissolved in water, 3 or 4 times daily after meals. Nausea may be prevented by small doses of menthol beforehand, e.g.,  $\frac{1}{10}$  gr. in 15 m. of tincture of orange.

A white, crystalline powder obtained by mixing solutions of equimolecular proportions of sodium theophylline and sodium acetate and evaporating to dryness. Contains not less than 55% of anhydrous theophylline (*U.S.P. XI*, 55 to 65%).

**Soluble** 1 in about 25 of water; insoluble in alcohol 90%, ether or chloroform.

**Incompatible** with acids, ammonium salts and sodium bicarbonate.

**Uses.** A soluble compound for the administration of theophylline.

**Theophyllina cum Æthylenediamina** (*U.S.P. XI*). **Syn and Prop. Name.** AMINOPHYLLINE, METAPHYLLIN, EUPHYLLIN (*Byk Gulden Werke, Berlin; Whiffen, London*) (in tablets containing 1½ gr., suppositories containing 5½ gr. and ampoules containing about 7½ gr.).

**Dose.**—Orally, 1½ to 3 grains (0.1 to 0.2 g.) thrice daily; rectally, 5½ grains (0.36 g.) as a suppository or retention enema, intramuscularly, 7½ grains (0.48 g.) in 2 ml. 3½ grains (0.24 g.); may be given intravenously in emergency in 10 ml. of sterile water *U.S.P. XI* average dose 1½ grains.

White or slightly yellowish granules with a slight ammoniacal odour and bitter taste. Contains 70 to 80% of anhydrous theophylline. To be stored in air-tight containers.

**Soluble** 1 in 5 of water (at 25°); insoluble in alcohol and ether.

**Uses.** Has the properties of theophylline with the advantage of greater solubility and consequently greater rapidity of action. In addition to its use as a diuretic in cardiac and renal œdema and eclampsia, the compound is also of value in post-operative retention of urine, cardiac asthma and angina pectoris. It promotes

coagulation of the blood and has been found useful in hæmoptysis and other hæmorrhages.

**ANGINA PECTORIS.** In almost every case of paroxysmal heart pain aminophylline can be depended upon to give relief no matter how acute the attack, and even when true coronary embolism appears to be the cause.—J. F. Quigley, *Prescriber*, 1935, 205.

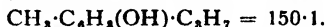
**Bassia (B.P.C.).** *Syn.* MOWRAH, MOWRA, ILLIPE.

The seeds of *B. latifolia*, *B. longifolia* and *B. butyracea*, containing 50 to 55% of a semi-solid pale yellow fixed oil with unpleasant taste and odour. When bleached by light and air the product is mowrah butter (illipe butter), used as food in India and for the manufacture of chocolate. The powdered cane remaining after expression of oil is mowrah meal. It contains the poisonous saponin, mowrin, and is used as a worm-killer for lawns (4 oz per sq. yard). The hardened fat is used in margarine manufacture.

**Shea Nuts and Shea Butter.** From the Shea tree, *Butyrospermum Parkii* (Sapotacæ), a native of W. Africa. The pulp of the fruit is eaten by the natives and by animals. The nuts are  $1\frac{1}{4}$  in in length and 1 in in diameter, with shells of a light brown colour; the dry kernel is firm and of a dark chocolate-brown colour and varies in weight from 3 to 5 g. The "butter," when clean and well prepared, is greyish or yellowish-white, has a not unpleasant odour, and consists of oleic acid 60%, stearic acid 30 to 35%, and lauric acid 3 to 4%. Used largely as food in W. Africa, and in Europe in candle and soap-making. The nuts grow in immense quantities on the Gold Coast.—*Bull. imp. Inst., Lond.*, 1912, No. 2.

## THYMOL

*B.P.*, *U.S.P. XI*, *P. Helv. V*, *P. Dan.*, *P. Belg. IV*, *P. Ital. V*



*Syn.* ACIDO TIMICO (*F.E. VIII*), 3-METHYL-6-ISOPROPYLPHENOL.

**Dose.**— $\frac{1}{2}$  to 2 grains (0.03 to 0.12 g.), in pills with soap and a trace of alcohol, or in oily or aqueous solution. *Anthelmintic dose.*—15 to 30 grains (1 to 2 g.). *U.S.P. XI* states 30 gr. divided into 3 doses. *F.E.* states maximum in 6 hours 1 to 2 g. It is best given finely powdered and mixed with sodium bicarbonate or lactose to prevent agglomeration of the particles.

Occurs in colourless crystals with characteristic pungent odour and taste. Prepared synthetically from piperitone obtained from the oil of *Eucalyptus dives* or extracted from oils of thyme, *Monarda punctata*, or ajowan, *Trachyspermum Ammi*.

Oil of thyme contains 20 to 30% of thymol, *Monarda punctata* oil contains about 60%, and ajowan oil 45 to 55%.

Owing to competition of synthetic thymol, it is no longer profitable to prepare natural thymol from Indian ajowan seed. Ajowan seed grown in Seychelles gives twice the yield of oil of Indian seed.—*Imp. Inst. Rep.*, 1929.

**Soluble** 1 in 1500 of water, 1 in 200 of glycerin, 1 in 8 of alcohol and glycerin, equal parts; soluble in fats and oils, and 8 in 3 of alcohol 90%, and freely soluble in ether, acetic acid and caustic alkalis. Liquefies with menthol, chloral hydrate, camphor and phenol.

**Uses.** Externally a powerful antiparasitic, also for certain stages of eczema and psoriasis and for broken chilblains (*see* Unguentum) and for burns (*see* Volckmann's solution). A powerful

antiseptic. It is also a good deodorant. May colour the urine green. The administration of a solvent of thymol, e.g., alcohol, simultaneously with or immediately after a large dose should be avoided.

A 5% alcoholic solution of thymol has been used in place of iodine tincture for sterilising the skin prior to operation. Two applications are made with an interval of 5 minutes; 3 minutes after second application the operation may be started. A 10% alcoholic solution is effective in tinea capitis.

As an antiseptic lotion or mouth-wash a 1 in 2000 solution may be used (see also *Glycerinum Thymolis Compositum*; or *Liquor Thymolis Compositum*). It is a common ingredient of sprays for catarrh.

**ANKYLOSTOMIASIS.** Thymol is an anthelmintic for hookworms. It is best administered in a cachet or capsule in a dose of 30 gr. for an adult, repeated in 2 hours, and followed after another 2 hours by a saline purge. Food and solvents of thymol (e.g., alcohol) must not be taken until the purge has acted. Sodium bicarbonate should be taken for 3 days before the treatment.

In large doses causes gastro-intestinal irritation, tinnitus and deafness, dyspnoea with slowing of respiration, acceleration and then slowing of pulse and fall of temperature. It is best given with equal quantity of lactose or sodium bicarbonate.—*J. Amer. med. Ass.*, 1/1929, 744

Extensive experience indicates maximum dose of 60 gr. for a healthy adult man and 45 gr. for a woman, and in pregnant women, or cases with very bad infection, and in elderly patients, or those with heart disease, or extreme debility, 30 gr. or less, the dose being given in two or three divided doses of 15, 20 or 30 gr. each at one- or two-hour intervals, followed by a strong saline purge. Do not repeat in less than a week, and prohibit alcohol, fats, vinegar, and other solvents of thymol on day of treatment. The dangers of thymol are overrated, but untoward effects in patients with chronic disease of the intestine and in oedematous patients. Most effective on hookworms, but usually fails to remove heads of tapeworms.—R. N. Chopra and A. C. Chandler, *Anthelmintics and Their Uses* (Ballière, Tindall & Cox, 1928)

Ankylostomiasis treated by  $\frac{1}{2}$  dr dose of betanaphthol and thymol  $\frac{1}{2}$  dr in a one-ounce draught, repeated.—H. G. Phippen, *Brit. med. J.*, 1/1923, 371.

Thymol, 3 cachets of 15 grains, given at intervals of 2 hours—routine treatment.—N. Cantlie, *J. trop. Med. (Hyg.)*, 1923, 42

Thymol was in greatest use when prolonged examination aimed at, and must often have succeeded in disclosing, deworming. For successful use it must be particulated. Thymol crystals readily set into a solid mass, so that when packed into a digestible capsule its shape may still be recognised in the now bare lump of wasted thymol passed in the fæces. Proper dispensing quite alters matters. B. E. Washburn and G. C. Payne showed in Trinidad nearly twenty years ago that when the drug was finely ground and then intimately mixed with at least an equal quantity of sugar of milk, deworming after two treatments increased from 12.6% to 49.1%. On available evidence it may be concluded that two courses, each of 60 gr. of "finely particulated" thymol, will effect deworming in about 50% of adults. Moreover, such deworming is safe in those not already moribund or nearly so. Howard (1919) pointed out how persistently it was stated that 60-grain adult doses of thymol were dangerous, but there had actually been given over a million such doses in the United States with no death. Actually, thymol is as safe as it is because, like alcohol, it is apt to produce early symptoms of intoxication, and the intoxicating dose is far removed from that which kills. Methods of drug appraisement of the treatment of hookworm seem to leave thymol in the first place when safety and efficiency are both considered.—C. Lane, *Lancet*, 1/1935, 1461.

**Gargarisma Antisepticum (Mid. H.).**

Boric acid 6 gr., thymol  $\frac{1}{2}$  gr., oil of eucalyptus  $\gamma_{10}$  m., oil of peppermint  $\frac{1}{2}$  m., glycerin 24 m., fuchsine q.s., water to 1 oz. A useful general gargle.

**Glycerinum Thymolis Compositum (B.P. C.)***Syn.* GLYCERINUM THYMOL ALKALINUM.

A solution containing sodium bicarbonate, borax, sodium salicylate, menthol and thymol with other aromatic antiseptics

**Liquor Thymolis.** 1 in 800 of warm water

This saturated aqueous solution is used diluted as an antiseptic gargle, undiluted it is too strong

**Liquor Thymolis Compositum (B.P.C.)***Syn.* LIQUOR ANTISEPTICUS.

Contains boric and benzoic acids, thymol and eucalyptol with other aromatic antiseptics

**Mistura-Oleo-Balsamica.** *Syn.* BALSAMUM VITÆ HOFFMANNI, "TINCTURE OF LIFE." *Dose* —1 to 4 drachms in water.

Oils of lavender, thyme, lemon, nutmeg and orange-flowers, of each 4, oil of clove and cinnamon of each 3½, balsam of Peru 10½, alcohol 90% to 1000, allow to stand a few days, then filter

A remedy for snake bites    A carminative stimulant

**Pigmentum Thymolis.**

Thymol 1, ether 10, and alcohol 90% 5, used as pigment in ringworm of the scalp—whilst acting as parasiticide it dissolves the fat, loosens the hairs and thus helps epilation    2½ to 5% in a mixture of chloroform and olive oil is also used

**Sapo Thymol (St G H.)**

Thymol 5 gr, soft soap ½ oz, alcohol 90% to 1 oz

**Spiritus Thymolis.** *Dose.*—3 to 15 minims (0.2 to 1 ml)

Thymol 1, alcohol 90% to 10, for medicating the wool of respirators    In scabies, where the infection is limited and recent, this solution is suitable for short applications

**Volckmann's Thymol Solution.**

Thymol 1, alcohol 90% 20, glycerin 20    Dissolve and add to water 1000    Used as a spray and antiseptic lotion, *e.g.*, for burns.

**Unguentum Thymolis.**

Thymol 20 gr., soft paraffin to 1 oz    Dissolved by heat    Used in the later stages of eczema and for other skin affections    Applied half strength to the skin keeps off gnats, etc

**Vapor Thymol (T.H.)**

Thymol 6 gr, alcohol 90% 1 dr., light magnesium carbonate 3 gr., water to 1 oz.    A teaspoonful to a pint of water at 140°F. for inhalation.    A strong stimulant.

**Angicid (Richter, London)** Mouthwash tablets containing thymol, menthol, caryophyllum and peppermint oil.

**Borol (Parke, Davis, London)** Borate, bicarbonate and benzoate of sodium with eucalyptol, menthol, oil of pine, etc    For use as a gargle, mouthwash and spray, or for vaginal injection

**Eubrol (Parke, Davis, London).** Euthymol and fluid extract of red gum Mouthwash.

**Euthymol (Parke, Davis, London.)** Eucalyptol, oil of wintergreen, menthol, thymol, benzoic acid and boric acid.    Liquid mouthwash, gargle, etc.

**Glycothymoline Brand Solution (Kress & Owen, New York, Christy, London).** "Borax 2.010, thymol 0.037, orcelli 0.123, menthol 0.037, benzol hydrate 1.68, Ol. Betulæ Lentæ 0.030, Sod. acid carb. 2.346, S.V.R. 4.085, glycerin 16.749, cajeputol 0.075, distilled water 72.708, Hyd. Oxvbenz. 0.074, Ol. Pumi Ess. 0.037."

**Thymaglycine (Martindale, London).** Antiseptic solution containing sodium benzoate, glycerin, menthol, essential oils, and thymol    As such, or

diluted, is beneficial in rhinitis, pharyngitis, quinsy, and in gastric and intestinal catarrh. *Dose*.—10 to 30 minims (0.6 to 2 ml.).

**Zymocide** (*Reed & Carnrick, New Jersey, Coates & Cooper, London*). Antiseptic germicide containing thymol, eucalyptol, menthol, methyl salicylate, boric and benzoic acids. For use as a spray, gargle and mouthwash and for local application.

**Thymolis Iodidum** (*B.P.C., U.S.P. XI*).

$(C_6H_5)(CH_3)(C_2H_5)OI_2 = 550.0$ . *Syn. and Prop. Name* DITHYMOL DIIODIDE, ARISTOL (*Bayer Products, London*).

Reddish-brown or brick-red powder with slight aromatic odour; almost tasteless. Contains not less than 40% of I.

**Insoluble** in water, alcohol, glycerin, sodium hydroxide solution; soluble almost completely 1 in 10 of ether, also 1 in 50 of chloroform and in collodion, soft paraffin and fixed and volatile oils.

**Incompatible** with alkalis, mercuric chloride, metallic oxides or anything decomposing iodides.

**Used** for psoriasis, lupus, eczema, and for ozæna; as dusting powder (as an iodoform substitute) alone or diluted 5 to 50%. Ointments 2 to 10% and pastes also employed. For blepharitis and conjunctivitis 10% in sterile sesame oil solution is suggested, also for burns and ulcerations. For skin ulcers with equal weight of exsiccated ferrous sulphate Suppositoria (theobroma basis), 1 gr in 15 gr, for hæmorrhoids.

**Thymi Herba** (*R.P.C., P. Helv V, P. Dan*)

The dried flowering tops of thyme, *Thymus vulgaris* (*Labiatae*)

**Elixir Thymi** (*B.P.C.*)

*Dose*.—1 to 2 drachms (4 to 8 ml.).

Contains ammonium bromide 2 gr and liquid extract of thyme 7½ m per dr. with spirit of chloroform, glycerin, treacle and syrup. For whooping cough.

**Extractum Thymi Liquidum** (*B.P.C.*) *Syn.* EXTRACTUM THYMI VULGARIS LIQUIDUM *Dose*.—10 to 60 minims (0.6 to 4 ml.) 1 in 1

**Syrupus Thymi.**

Liquid extract of thyme 1, syrup 7 *Dose*.—1 to 4 drachms (4 to 16 ml.)

**Oleum Thymi** (*B.P.C.*)

*Dose*.—1 to 5 minims (0.06 to 0.3 ml.)

Distilled from the fresh herb. A dark reddish-brown liquid containing not less than 40% of phenols (thymol and carvacrol) Used in whooping cough and bronchitis, and externally as a rubefacient

"Red" thyme oil on rectifying is converted into white thyme oil, which contains 20 to 30% of phenols.

Oil of red thyme is obtained from the fresh herb *Thymus vulgaris* and other varieties in southern France. Spanish thyme oil is probably derived from a species of *Origanum*.

**Oleum Ajowan** (*B.P.C.*). *Syn.* PTYCHOTIS OIL. *Dose*.—¼ to 3 minims (0.03 to 0.2 ml.). The oil distilled from the fruits of *Trachyspermum Ammi*, containing not less than 40% of thymol. Used in India as a carminative

**Oleum Majoranæ**, from *Origanum majorana*, contains practically no phenols

**Oleum Origanum**, from *O. hortum* and *O. majoranoides*, may contain up to 85% of carvacrol.

**Karvol** (*Crookes Laboratories, London*) A mouthwash and gargle containing chlor-carvacrol as a basis. Also prepared as a dental cream, inhalant, liniment, insect-bite lotion, etc

## THYROIDEUM

*B.P., U.S.P. XI, etc*

*Syn.* THYROIDEUM SICCUM, DRY THYROID, THYROID EXTRACT, THYROID GLAND, THYROIDINE (*P. Belg. IV*).

[P1] "*Thyroid gland, the active principles of; their salts.*"

[86] "*Thyroid gland, the active principles of, their salts—specify proportion as either*

(a) *the proportion of thyroid gland contained in the preparation; or*

(b) *the amount of thyroid gland from which a specified quantity of the preparation was obtained together with an indication whether the amount relates to fresh or to dried gland.*"

[87] *Medicines made up ready for the internal treatment of human ailments containing—Thyroid gland, the active principles of; their salts—must be labelled with the words "Caution. It is dangerous to take this preparation except under medical supervision."*

*Dose* — $\frac{1}{2}$  to 5 grains (0.03 to 0.3 g.).

For method of assay and notes on variations in iodine content see Vol II, p. 199, 20th edition.

To avoid confusion, it should be borne in mind that thyroid *B.P.*, though standardised to 0.1% of iodine in combination as thyroxine, actually contains more than 0.2% of total iodine. Of the three iodines present in thyroid, only one, acid-insoluble thyroxine iodine, is recognised in the *B.P.* product, and it is on thyroxine iodine content solely that the *B.P.* standardisation is determined. —Armour & Co, *Brit. med. J.*, ii/1932, 780.

In view of the increasing demand for 5-grain tablets of thyroid extract, it should be realised that the *B.P.* preparation "Thyroideum," is five times as strong as the fresh gland preparation. Complaints from doctors and chemists of untoward effects following the use of 5-grain thyroid tablets showed on enquiry that fresh gland was intended to be used. Unless fresh gland is specifically asked for there is almost a certainty of the stronger extract being supplied —*Brit. med. J.*, i/1934, 1039.

Obtained from the thyroid glands of ox, sheep and pig. After removal of connective tissues and external fat the glands are dried below 60°, powdered, and fat extracted by light petroleum. The product is diluted with lactose to contain 0.09 to 0.11% of iodine in combination as thyroxine.

Glandulæ Thyroidæ siccatae (*P.G. VI*) contains not less than 0.18% of iodine, with precise methods of detection of adulteration with iodine compounds. *P. Ned. V* specifies that thyroid must be desiccated at 30° and adjusts to 0.3% of iodine with lactose. *F.E. VIII* specifies sheep, ox or other animal used for human food, with 0.2% of combined iodine. *P. Ital. V* is similar. *Thyroideæ siccata (P. Helv. V)* contains from 0.08 to 0.1% thyroxine, not more than 2% fat, 8.5% moisture and not more than 5% ash. *U.S.P. XI* requires 0.17 to 0.23% of iodine in thyroid combination and absence of iodine in inorganic or any form of combination other than that peculiar to the thyroid gland.

The thyroid gland is situated in the neck and consists of two lobes, one on each side of the upper part of the trachea and larynx, joined by an isthmus. In man the gland weighs about 25

grammes and the average length of each lobe is 2 inches. It is larger in the female than in the male. One lobe ( $\frac{1}{2}$  gland) of the sheep's thyroid weighs on an average about 35 grains and yields about 9 grains of dry thyroid. Histologically the thyroid has an external capsule of dense connective tissue which sends trabeculae into the interior, dividing it into irregular lobules. The lobules consist of groups of closed oval or spherical vesicles connected by areolar tissue and lined by a single layer of columnar epithelium. The vesicles contain a yellow viscid fluid called colloid.

Microscopically, powdered desiccated thyroid shows smooth or striated hyaline fragments of colloid, some of which contain granules, minute vacuoles, crystalloidal bodies and cells with numerous irregular fragments of follicular epithelium, both of which stain brown with a mixture of Mallory's stain and 1% solution of phosphotungstic acid.—H W Youngken, per *Pharm. J.*, i/1936, 44.

Histological variations occur in thyroids from animals of different ages. In younger animals the glands are usually hyperplastic, with small acini and little colloid. In older animals the acini tend to become larger with more colloid.—Abbott and Prendergast, *Canad med Ass J*, ii/1934, 465

The gland normally contains about 10 or 15 mg. of iodine. Three iodine-containing compounds may be obtained from the gland—thyroxine, diiodotyrosine and iodothyroglobulin. Opinion is changing to the view that total iodine is a better guide to activity than thyroxine iodine. The effect produced by intravenous or subcutaneous injection of thyroxine is the same as that of thyroid, but when thyroxine is given by mouth its therapeutic effect is less than that of thyroid in equivalent amount. The disodium salt of thyroxine has an action similar to that of thyroid. The monosodium salt (thyroxine-sodium *B.P.*) is considerably less effective. The effect of thyroxine given by mouth probably depends upon the solubility of the salt administered.—W. O. Thompson *et al*, *Endocrinology*, 1934, 228.

A synthetic compound, 3·5-diiodothyronine, appears to have all the physiological properties of thyroxine although it is much weaker, about 50 mg. being required to give the effect of 1 mg. of thyroxine. It is stable, soluble and easily absorbed.—*Prescriber*, 1934, 155; 1935, 148

**Physiology.** The principal function of the thyroid gland is to increase oxidation processes in the body, thus all body activities are influenced by the state of the thyroid. Deficiency of thyroid secretion results in a fall in heat production—*i.e.*, decrease in the rate of metabolism and general loss of mental and physical vigour. The pulse is slower, the skin becomes dry and thickened in the subcutaneous layers. Congenital thyroid deficiency leads to the condition of cretinism, characterised by poor mental and physical development. Deficiency in the adult results in the condition termed myxœdema. Excess of thyroid secretion increases the basal metabolic rate, body tissues are burned up with the result that the individual becomes thin. Mental activity is increased and the rate of the heart beat is quickened.

The thyroid is the gland of creation. Has anyone ever heard of a myxœdematous creator? Crichton Miller asks again for subthyroidic artists—be it of works or of children. The woman of artistic ability ceases to create works of art as soon as she is taken up with the maternal function.—*Brit. med. J.*, ii/1922, 552.

Injectons of thyroxine or oral administration of thyroid gland to rats causes increased excretion of calcium in faeces and a negative calcium balance. This is corrected by administration of calciferol or irradiated ergosterol.—L. I. Pugsley and E. Anderson, *Biochem. J.*, 1934, 1135

Injectons of thyroxine in cows causes increased secretion of milk and increase of milk fat.—W. R. Graham Graham, *Biochem. J.*, 1934, 1368

A new conception of the thyroid gland. The Applied Anatomy and Physiology of the Thyroid Apparatus—G. S. Williamson and I. Pearce, *Brit. J. Surg.*, 1926, 466, *Brit. med. J.*, 1/1926, 625. For a criticism of these authors' views see Rienhoff, quoted by A. T. Cameron, "Recent Advances in Endocrinology" (Churchill), also Marine (*see below*).

For an account of the physiology of the thyroid and its relationship to other endocrine glands, *see* D. Marine, *J. Amer. med. Ass.*, 1/1935, 2250. The following is a summary—

The functioning of the thyroid gland is intimately related to the amount of iodine in the diet—deficiency of iodine leads to enlargement of the thyroid, as seen in endemic goitre. Diets rich in protein and fats increase the rate of discharge of thyroxine from the gland and lead to enlargement. Rickets-producing diets (*i.e.*, diets low in phosphorus and high in calcium or *vice versa*) cause thyroid enlargements in dogs and cats if the iodine intake is low.

The activity of the thyroid gland is influenced by the action of other endocrine glands in the body. The anterior lobe of the pituitary gland contains a thyroid-stimulating or thyrotropic substance which can be extracted by aqueous alkali. Removal of the thyroid gland from animals leads to enlargement of the anterior pituitary. Persons with large parathyroid glands have enlarged anterior pituitaries. The thyroid and pituitary glands are delicately balanced. Any deficiency in the thyroid secretion quickly stimulates the pituitary, either directly or by way of a nervous mechanism, to produce more thyrotropic hormone. Conversely, supplying the thyroid hormone reduces anterior pituitary activity.

Enlargement of the thyroid occurs during menstruation and pregnancy, this fact, together with the frequency of goitre at puberty and the menopause, suggests a relationship of thyroid function with that of the gonads. Removal of the gonads from animals results in a depression of thyroid function. Administration of thyroid has an inhibitory effect on oestrus. Contradictory results on thyroid activity have been reported from the administration of oestrin; some workers report increased thyroid activity, others the opposite effect. The influence of the thyroid on the gonads is probably exerted through the medium of the anterior pituitary.

The thyroid appears to neutralise the action of insulin. Thyroidectomised dogs are less sensitive to the hyperglycaemic action of adrenaline than normal dogs.—J. H. Burn and H. P. Marks, *J. Physiol.*, 1925, 131.

Thyroidectomy increases the sensitivity of sheep to the action of insulin.

The thyroid hormone promotes glycogenolysis and hence the hypoglycaemic effect of insulin is increased after thyroidectomy and decreased by thyroid feeding. This effect may be due to its sensitising effect on the action of adrenaline on the sympathetic nervous system.

There is much evidence to support the view that the thyroid hormone increases the irritability of the sympathetic nervous system or in some way sensitises the tissues innervated by it, so that they are more susceptible to stimulation by adrenaline.

The adrenal cortex and the sex glands acting through the anterior pituitary exercise some regulatory or inhibitory control over thyroid function. When this control is decreased or withdrawn the activity of the thyroid is temporarily increased.

The most characteristic physiological effect of thyroid—or of thyroxine—is that it increases the oxidation of carbohydrates, proteins and fats in the body after a latent period of about 12 hours; it also increases the excretion of calcium and magnesium. Although the mechanism of the increased oxidation in the tissues is unknown, there is evidence that adrenaline and thyroxine may work together in the process.—D. Marine, *J. Amer. med. Ass.*, 1/1935, 2253.

Biochemical basis of thyroid function—C. R. Harington, *Lancet*, 1/1935, 1197, 1267.

### Tests for Thyroid Activity

BASAL METABOLIC RATE (B.M.R.) means the rate of energy



exchange in the body as seen under basal conditions (after elimination of movement, digestion, etc.). A relatively simple way of determination (as described by Benedict, *J. Amer. med. Ass.*, ii/1921, 247; and Krogh, *Brit. Ass. Rep.*, 1921, 445) is to measure the oxygen consumption of the patient during a given period. Oxygen is rebreathed in a closed-circuit apparatus in which the exhaled  $\text{CO}_2$  is absorbed; the diminution in volume of the gas indicates the amount of oxygen consumed. The B M R. does not vary as much as 10%. In hyperthyroidism it rises to 25 or 50% above normal, or even more; while in deficiency the rate falls below normal. Boothby has calculated that, to maintain it at normal, 12 to 14 mg. of thyroxine must be present in the system. The thyroxine is used up at the rate of about 0.5 mg. a day. In a case of myxœdema this amount would have to be given daily intravenously. The equivalent of *Liquor Thyroidæ* (B.P. '98) estimated to be 10 minims or 5 grains of fresh gland.—*Prescriber*, 1922, 345, and 1924, 192; *Lancet*, i/1923, 131; G. R. Murray, *Clin. J.*, Aug., 1923, 362.

Determination and interpretation.—H F Moore, *Lancet*, i/1925, 219. See also J. D. Robertson, *Practitioner*, ii/1935, 780.

Many cases of hyperthyroidism are diagnosed as neurasthenia and treated with tonics with little improvement. Determination of the B.M.R. will easily differentiate hyperthyroidism from other conditions.—H W. Riggs, per *Prescriber*, 1924, 188.

**Goetsch's Adrenaline Test** depends upon the fact that the sympathetic nervous system in cases of hyperthyroidism is specially sensitive to adrenaline. Blood pressure, pulse rate and respiration rate are recorded at intervals after the subcutaneous injection of 0.5 ml of adrenaline chloride solution. A rise of blood pressure, with an increased pulse and respiration rate, is considered diagnostic of hyperthyroidism.

THE "IMPEDANCE ANGLE" as a test for the diagnosis of diseases of the thyroid gland. In constant-current work the impedance of the body (*i.e.*, resistance due to self-induction) is measured by a single factor, namely, the resistance; but with alternating currents the body functions as a condenser as well. It is the ratio of these two factors, termed the impedance angle (I.A.), which shows variations in disease of the thyroid. The author describes a comparatively simple apparatus which gives direct readings of this value. The patient, seated in a chair, has each arm immersed in a 10-litre bath of 1% saline at 25°. Alternating current of low intensity is passed through the patient into a simple bridge circuit. The impedance offered by the body is balanced on the bridge by adjusting a variable resistance and condenser. The impedance angle is increased in thyrotoxicosis; in non-toxic goitres it is generally lower than normal. This test is claimed to be more specific and certain than B.M.R. determination.—M. A. B. Brazier, *Lancet*, ii/1933, 742. See also *1 Instn elect Engrs*, 1933, 203.

**Estimation of blood cholesterol** as a guide to thyroid therapy. Crestinuria occurs before any change in B M R. is noted, and is a delicate index of the effect

of thyroid treatment.—J. E. Hess, *Ann. Int. Med.*, 1934 (Nov.), 607. Also Gilligan, *ibid*, 1934, (Nov.), 84, 748.

**Iodine tolerance test** of value in diagnosis of a typical hypothyroidism—A. W. Elmer, *Endocrinology*, 1934, 487.

**Quinine Test.** From a series of more than 4000 cases it appears that the quinine test for thyrotoxaemia is a dependable guide in diagnosis, the frequency of error not exceeding 5%. The tolerance for quinine in hyperthyroidism appears to vary in direct proportion with the height of the basal metabolism rate, and is fairly parallel with it, serving as a guide to progress under treatment. Depending on the severity of active hyperthyroidism, patients are able to take 30 grains or more of quinine sulphate or hydrobromide daily for weeks without evidence of cinchonism. It is as dependable as the basal metabolic rate and as accurate a guide in treatment. It does not discriminate between toxic adenoma and exophthalmic goitre.—*J. Lab. clin. Med.*, 1935, 21, 123.

**Toxic Effects.** Over-doses of thyroid preparations may cause rapid pulse, "racing" of the heart, feverishness, headache, pruritus, and even delirium. Chronic thyroid poisoning has also been observed—the symptoms being emaciation, muscular weakness, loss of hair, dilated pupils and general debility.

A single large dose of thyroid fed to goats produces no effect; the same quantity in small amounts over a period produces symptoms—Prof. A. J. Clark, *Brit. med. J.*, 11/1925, 847.

Experimentally it has been confirmed that prolonged excessive thyroid administration reduces the glycogen store in the liver; this is due to an increased utilisation rather than to decreased storage capacity.

From tests on dogs and rats it is deduced that toxic effects from thyroid or thyroxine administration can be overcome by treatment with salts of copper, iron, arsenic and nickel.—Hesse-Vonderlinn and Zippmeisel, *Arch. exp. Path. Pharmacol.*, 1933, 173, 192.

Unilateral exophthalmos following use of thyroid in a case of myxoedema. 12½ grains daily taken during a year.—T. Gillman Moorhead, *Brit. med. J.*, 1/1931, 442.

Very rarely the administration of thyroid extract for the treatment of myxoedema, the relief of obesity, or some other purpose, is followed by the development of exophthalmos, and an example of this is reported. It is probable, therefore, that when exophthalmos follows the administration of thyroid extract, this is not a direct result of the action of the thyroid extract, but is due to some other substance which in certain rare individuals is produced in response to thyroid extract. Experimental evidence suggests that the substance may be the thyrotropic hormone of the pituitary.—W. Russell Brain, *Lancet*, 1/1936, 186.

**Thyroid Addiction.** Details of three cases of thyroid addiction. The symptoms of excessive intake were loss of weight, fall in blood pressure, excitement and other indications of thyrotoxicosis. Keogh points out that the administration of thyroid hormone in sufficiently large amounts leads to a thyrotoxic condition resembling in many ways exophthalmic goitre.—S. W. Patterson, *Brit. med. J.*, 11/1934, 6.

**Goitre.** Enlargement of the thyroid gland may be simple or non-toxic, or toxic, malignant or inflammatory. Simple goitre is a compensatory enlargement of the gland which occurs when the amount of thyroid tissue is insufficient to supply the quantity of hormone necessary for the needs of the body—whether as a result of reduced iodine consumption or of increased demands elsewhere in the body. This enlargement appears to be the direct result of stimulation by the thyrotropic hormone of the anterior pituitary and is accompanied by changes in histological structure and a decrease in the amount of colloid. Endemic goitre is the term applied to a simple enlargement of the thyroid seen constantly in certain mountainous districts. Although the exact cause of endemic goitre is a matter of controversy, it is probably the result of an iodine insufficiency and can be entirely prevented with iodine or iodides (*q.v.*).

The size of the thyroid fluctuates—there is a continuous variation throughout life and a phase-variation at specific periods of life and under physiological strain. Day-to-day variations are to be anticipated. The thyroid is the best "indicator of dietetic deficiencies." Where a food deficiency interrupts the normal process of growth a goitre is liable to appear. Diets deficient in fat seem to lead to

storage of a colloid very deficient in iodine—or the storage of a very dilute iodine without reduction of the total iodine stored. Scorbatic diets produce a gland yielding a high concentration of iodine as well as a high total iodine store. There are thus at least two possible variables in the material stored by the gland—the iodine and the colloid, each of which may vary independently of the other. The “iodine hypothesis” which seeks to explain all the thyroid function cannot be sustained. Iodine deficiency in the environment may contribute to the incidence of goitre but it is not the cause of goitre. The deduction is that both the environments and individual deficiencies in iodine are the common result of some undiscovered factor.—*The Life Line of the Thyroid Gland*, Col. R. McCarrison. Leader, *Brit. med. J.*, ii/1932, 718.

**Uses.** Thyroid and preparations made from the thyroid gland have been employed for relieving cretinism and myxœdema. Myxœdema is speedily improved by thyroid, and a more or less complete cure is established. The patient must continue to take the preparation more or less all his life. “The results,” says Osler, “are unparalleled by anything in the whole range of curative measures. Within a few weeks a poor, feeble-minded, toad-like caricature of humanity may be restored to mental and bodily health.” The original case of myxœdema first treated years ago by Murray with *Liquor Thyroides* (hypodermically) enjoyed health by taking 10 minims of the solution each day—6½ ounces in the course of a year, for 28 years.

V. Horsley had, previously to Murray's work, practised transplantation of sheep's thyroid gland into the tissues of a myxœdematous patient. Later McKenzie showed internal use of thyroid preparations equally good. Atrophy of the thyroid need not shorten life provided this substitution treatment be fully maintained.—*Brit. med. J.*, i/1920, 359.

**CRETINISM.** Thyroid treatment. Results vary from complete idiocy to normality.—A. E. Naish, *Lancet*, i/1925, 91.

As soon as cretinism is recognised or even suspected treatment should be started. Thyroid should be given in very small doses at first and increased rapidly, if it is well tolerated. It is best to begin with ½ gr. twice daily, and after three days give it three times a day. Then the dose is increased every week until 1 gr. is given three times daily. Improvement is rapid and should be very obvious in three or four weeks. The optimum dose varies. There should be a steady gain in weight, regular action of the bowels, and no disturbance in general health. Loss of weight and diarrhoea are the two most useful indications of overdosage. Occasionally a baby is very intolerant even of the smallest dose, and with every increase much loss of weight, diarrhoea and general disturbance of health take place. In such cases it is necessary to proceed with extreme caution, allowing the child time to recover the lost weight and add a little more before any further increase in the dose is made. Thyroid must be administered without intermission and as soon as a child is old enough to co-operate it is useful to have an estimation of the basal metabolic rate. In general the earlier treatment is begun the better the outlook, and it is for this reason that early diagnosis is so important. It is true that so long as treatment has been started in the first year or two the physical signs of cretinism disappear entirely, but the effect on the mental development is much less satisfactory. Even in babies who have had an adequate dose of thyroid from the second or third month onwards the result is sometimes most disappointing and the intelligence may be subnormal or even abnormal. The majority always remain a little below the average in mentality, but some respond so well that they become indistinguishable either mentally or physically from normal people of their own age. Even in the case of cretins treated for the first time between the ages of one and three years the response is sometimes unexpectedly good. If, however, the treatment is not instituted until the later years of childhood neither the appearance nor the mentality ever becomes normal, though the improvement in looks and height may be considerable.—E. A. Cockayne, *Fractitioner*, ii/1935, 767.

**SPONTANEOUS ACUTE MYXEDEMA.** Patient, female, age 63, complained of drowsiness, swelling of eyelids and increasing weight. Treatment was as follows: 15 gr. whole gland thyroid injected subcutaneously and 8 gr. given orally—the latter t.d.s. In 24 hours temperature rose, lethargy lessened. Dosage reduced to 4 gr. t.d.s. Mentally the patient became normal and a dosage of 2 gr. b.d.s. was maintained.—H. M. Watney and A. H. Douthwaite, *Brit. med. J.*, ii/1932, 1142.

**ULCERS** in the leg quickly healed under thyroid treatment (2 gr. t.i.d.) in a few weeks although they had not changed under other treatment for six years.—M. H. Cohen, *J. Amer. med. Ass.*, 1/1934, 283

For earlier references see previous editions

### SOME PROPRIETARY THYROID PREPARATIONS

[P1 87] **Anobese** (Paines & Byrne, London). Thyroid, anterior pituitary, thymus, ovary (or testes), and lymphatic substance. Capsules or ampoules ("M" or "F"). Dose—3 to 6 capsules daily with 2 or more injections weekly. Obesity of the "water-logged" type.

[P1 87] **Cavolysin** (Cavendish Chemical Co., London). Contains thyroid, anterior pituitary, thymus and testicular substance, for women, the testicular substance is replaced by ovarian. Supplied in tablets and in ampoules for intramuscular injection. For obesity.

[P1 87] **Elityran** (Bayer Products, London). Biologically standardised thyroid extract. Dose—1 or 2 tablets of  $\frac{1}{2}$  gr. thrice daily. Obesity, thyroid insufficiency, etc.

Production of Elityran outlined. Two iodine-containing protein fractions are separated from the thyroprotein by precipitation with saturated ammonium sulphate solution and dialysed.—*Endocrinology*, 1933, 13, 250

[P1 87] **Endothylin** (Endocrines Ltd., Watford). Each tablet contains  $\frac{1}{2}$  or  $\frac{1}{4}$  gr. of desiccated thyroid with magnesium phosphate, calcium phosphate (dibasic) and glycerophosphate, and potassium and sodium bicarbonates.

[P1 87] **Four Gland Tablets** (Martindale, London). Syn COMPOUND THYROID TABLETS (Martindale). 1 gr. each of thyroid, thymus, suprarenal and pituitary. Dose—One or two twice daily. Also available as an elixir containing the equivalent of 1 tablet per dr. [P1 87] **Three Gland Tablets** and **Elixir**, with suprarenal omitted, are also available.

[P1 87] **Glandiposan** (Richter, London). Tablets of thyroid B.P.  $\frac{1}{2}$  gr. and anterior pituitary  $\frac{1}{2}$  gr. Dose—1 tablet thrice daily. For obesity.

[P1 87] **Glandiposan Forte** tablets contain thyroid 3 gr. and anterior pituitary  $\frac{1}{2}$  gr.

[P1 87] **Hormonigen Tablets** (Hewlett, London). Contain thyroid, pituitary, ovary and testis. Dose—1 or 2 tablets before meals. In neurasthenia and for pluriglandular therapy.

[P1 87] **Hormotone** (G. W. Carrick, Newark, N.J., Brooks & Warburton, London). A combination of hormones derived from the thyroid, pituitary, gonad and suprarenal glands. Each tablet contains  $\frac{1}{2}$  gr. of desiccated thyroid and pituitary. Dose—One or two tablets thrice daily before meals, not more than six per day. Stated to increase mental, nerve, and muscular activity. Also available without post-pituitary.

[P1 87] **Incretone** (G. W. Carrick, Newark, N.J., Brooks & Warburton, London). Contains thyroid, pituitary and gonads. Dose—1 to 2 teaspoonfuls before meals. For use in asthenia, general debility, etc.

[P1 87] **Inkretan** (Promonta, Hamburg; Pharmaceutical Products, London). Tablets of thyroid and anterior pituitary lobe extract. For obesity.

[P1 87] **Iodobesin** (Anglo-French Drug Co., London). Tablets containing hepatic, pituitary, orchitic, ovarian, thyroid (deprived of lipoids), and suprarenal extracts, and iodalbumin. For obesity.

[P1 87] **Lipolysin** (Henning, Berlin, Pharmaceutical Products, London). "Male" contains thyroid, pituitary, pancreas, and testis. "Female" contains ovarian extract in place of testis. Dose—1 ml. intramuscularly 3 or 4 times weekly, and 1 to 3 tablets thrice daily. For obesity.

[P1 87] **Paromin** (Paines & Byrne, London). Preparation of thyroid standardised on its calorogenic activity, containing not less than 0.5% of natural organic iodine. In  $\frac{1}{4}$ -grain tablets and 1 ml. ampoules (5 gr. of fresh substance).

[P1 87] **Protonuclein** (*Reed & Carnrick, Jersey City; Coates & Cooper, London*). Tablets containing thyroid, suprarenal, lymphatic gland, brain, spleen, pancreas, thymus, with pepsin, salivary glands and excipients.

[P1 87] **Semboi** (*Napp, London*). Mixed gland tablets containing extracts of thyroid, thymus, pituitary (anterior), suprarenal and cerebrin, and orchis, with calcium glycerophosphate and phosphate of iron. Asthenia, impotence and premature senility. [P1 87] **Fiatal** tablets for women contain in addition extracts of ovary and mammary gland.

[P1 87] **Tetraglandular Tablets** (*Parke, Davis, London*). Desiccated suprarenal, pituitary, thyroid and parathyroid glands. *Dose*.—1 or 2 tablets.

[P1 87] **Thyracoids** (*Reed & Carnrick, New Jersey; Coates & Cooper, London*). Desiccated thyroid tablets

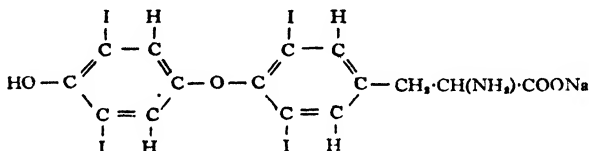
[P1 87] **Thyraden** (*Knoll, London; Pharmaceutical Products, London*). Stable thyroid extract (0.05 g. = 0.3 g. of fresh gland)

[P1 87] **Thyrafra Tablets** (*Parke, Davis, London*). Desiccated thyroid gland, desiccated suprarenal gland and Bland's pill. *Dose*.—1 tablet twice or thrice daily.

[P1 87] **Thyranon** (*Organon Laboratories, London*). Thyroid extract standardised chemically to 0.2% total iodine, and biologically.

[P1 87] **Thyroidin Elixir** (*Allen & Hanburys, London*). Contains the equivalent of 5 gr. of fresh thyroid in each dr. *Dose*.—1 to 4 drachms

[P1 87] **Thyroxinsodium** (B.P.)  $C_{15}H_{10}O_4NI_4Na = 776.8$ .



*Dose*.— $\frac{1}{160}$  to  $\frac{1}{4}$  grain (0.0001 to 0.001 g.). It is usually given by intravenous injection. The B.P. states that when thyroxine is ordered, thyroxinsodium may be dispensed.

The amount should be determined with reference to the B.M.R. It is calculated that 1 mg. of thyroxine causes an average increase of 2.8% in the B.M.R.—Gardner-Hill, *Lancet*, ii/1927, 621.

In patients previously treated with desiccated thyroid 1 mg. of synthetic thyroxine produces action analogous to that of 0.2 g. of the dried gland. The initial dose of thyroxine in the adult should not be more than 0.5 mg.—*Per Prescriber*, 1929, 158.

With a myxœdematous patient the maximum effect is produced on the tenth day after a single injection.

**Caution.** The action of thyroxine persists for 15 or 21 days. Wait until effect has passed off before giving a further injection.

The therapeutic use of thyroxine is limited by the necessity for intravenous injection as, owing to its extreme insolubility, it is absorbed irregularly when given by the mouth. Thyroxine probably exists in the gland as a constituent of a peptide or protein, but attempts to increase the solubility by preparing simple peptides containing thyroxine have, so far, been unsuccessful.—Ashley and Harington.

Thyroxinsodium is the monosodium salt of thyroxine, which is *dl*- $\beta$ -[3 : 5-diiodo-4(3', 5'-diiodo-4'-hydroxyphenoxy) phenyl]- $\alpha$ -aminopropionic acid. It contains 61 to 65% of I, and occurs as a white, crystalline powder sparingly soluble in water, more soluble in aqueous alkalis, forming unstable solutions. It is obtained by the action of a limited amount of sodium carbonate on thyroxine, which may be prepared synthetically or extracted from thyroid gland.

Prepared synthetically or extracted from thyroid tissue it is optically inactive. Exists in thyroid tissue as the *laevo* compound, which is physiologically more active than the *dextro* isomer.—Harington and Salter, *Biochem. J.*, 1930, 456.

Crystalline *laevo* thyroxine melts at  $235^{\circ}$  with decomposition.

**Preparation.** Extraction from thyroid gland using a dilute solution of barium hydroxide. Yield about 0.12% from the dry thyroid as compared with 0.0011% obtained by Kendall using sodium hydroxide—C. R. Harington, *Biochem. J.*, 1926, 293.

The thyroxine finally obtained is perfectly white (although the preparation of commerce is yellowish) and crystallises in rosettes or sheaves of fine needles which darken at  $220^{\circ}$  and melt with decomposition and evolution of iodine at  $231^{\circ}$  to  $233^{\circ}$ . Though thyroxine reproduces qualitatively the therapeutic action of thyroid it is stated not to be present therein but is produced during the process of extraction. Thus the nature of the thyroxine-yielding substance and the essential materials for its formation are still unknown. Originally it was believed that thyroxine was a derivative of tryptophane—a substance normally present in the circulating blood as a product of protein metabolism.

**Synthesis.** Hydroquinone monomethylether is combined with triiodonitrobenzene, yielding the diphenyl ether,  $\text{CH}_3\text{O} \cdot \text{C}_6\text{H}_4 \cdot \text{O} \cdot \text{C}_6\text{H}_2\text{I}_3 \cdot \text{NO}_2$ . The nitro group is successively changed into an amino group, cyanide group and an aldehyde group which is then condensed with hippuric acid. Hydrolysis with sulphuric acid and hydriodic acid yields the amino-acid,  $\text{HO} \cdot \text{C}_6\text{H}_4 \cdot \text{O} \cdot \text{C}_6\text{H}_4 \cdot \text{CH}_2\text{CHNH}_2 \cdot \text{COOH}$ . On iodising, thyroxine is produced. After purification the substance was found to have the properties of the natural thyroxine, both products being in the racemic form. Deiodothyroxine—a degradation product obtained by shaking thyroxine with palladium hydroxide in an atmosphere of hydrogen using calcium carbonate as a catalyst—is  $\alpha$ -amino- $\beta$ -4-(*p*-hydroxyphenoxy) phenylpropionic acid—the iodine atoms alone being replaced by hydrogen,  $\text{HO} \cdot \text{C}_6\text{H}_4 \cdot \text{O} \cdot \text{C}_6\text{H}_4 \cdot \text{CH}_2\text{CHNH}_2 \cdot \text{COOH}$ —C. R. Harington, *Biochem. J.*, 1928, 300; G. Barger, *Brit. med. J.*, i/1926, 1092, ii/1926, 1234, ii/1927, 861; *Lancet*, ii/1926, 192, i/1927, 719. *Pharm. J.*, i/1926, 734, ii/1927, 609. The isolation, chemical constitution and chemical synthesis of thyroxine—Prof. Barger, *Chem. & Drugg.*, ii/1927, 700. Synthesis of thyroxine—*Pharm. J.*, ii/1928, 363.

**Uses.** Thyroxinsodium is used for the same purposes as thyroid, and is given in cretinism, myxœdema and simple goitre.

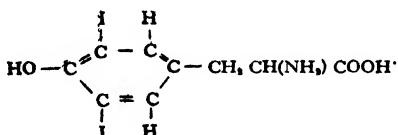
**OTOSCLEROSIS.** Based on the view that otosclerosis results from a diminished blood supply to the organ of hearing, due to the gradual failure of vasomotor response, this condition has been treated by the local application of thyroxine. The action of thyroxine applied locally is quite different from its usual therapeutic use, and causes an active congestion of long duration without inflammatory reaction. The tympanic membrane is anaesthetised with a freshly prepared 10% solution of cocaine in aniline, applied for 5 minutes and the canal mopped quite dry. Thyroxine  $\frac{1}{10}$  gr. dissolved in 4 m. of water is injected into the tympanic cavity at a point midway between the tip of the handle of the malleus and the posterior margin of the membrane. A gag placed between the teeth prevents the patient from swallowing and so opening the Eustachian tube, and the head is tilted backwards for 5 or 10 minutes immediately after the injection. In a preliminary report of 14 cases it is stated that about 50% of cases of otosclerosis and "dry middle-ear catarrh" can be greatly improved in regard to both hearing and tinnitus.—A. A. Gray, *J. Laryng.*, 1935, 50, 729.

In HYPOCHROMIC ANÆMIA, thyroxine increases the reticulocyte response to reduced iron.—S. van Beurden, *Ass. méd.* 1935, 13, 116.

[P1-87] **Thyroxinum** (U.S.P. XI) is the acidic substance containing not less than 64% of I as an integral part of the molecule.

*Average dose.*— $\frac{1}{10}$  grain.

[P1-87] **Diiodotyrosine.**



Dextrorotatory, colourless crystals containing 58.1% of iodine. Very sparingly soluble in cold water.

Has been used in the treatment of hyperthyroidism. In the preparation of patients for thyroidectomy diiodotyrosine induces remission, and reduction in basal metabolic rate.

No evidence to justify the conclusion that the effects are specifically different from those of iodine in other forms.—H. B. Gutman, E. B. Gutman, L. W. Sloan and W. W. Palmer, *J. Amer. med. Ass.*, 11/1933, 256.

The antithyroidal effect of diiodotyrosine is due merely to the iodine which is liberated from it; potassium iodide produces the same thyroid-inhibiting effect.—A. W. Elmer, *Quart. J. exp. Physiol.*, 1934, 24, 95.

Treatment of hyperthyroidism (Basedow's disease) with diiodotyrosine.—E. Thane, *Z. klin. Med.*, 1933, 123, 448.

[P1-87] **Diiodothyronine** (3 : 5). Symptoms of myxœdema relieved by 50 mg. of the disodium salt in 1 oz. of water daily—by mouth after food. No toxic effects observed after 2 or 3 weeks' treatment. B.M.R. restored to normal, loss of weight and pulse rate slightly raised. Effect of 50 mg. of diiodothyronine (as disodium salt) equivalent to that of 1 mg. of thyroxine.—A. B. Anderson, C. R. Harington and D. M. Lyon, *Lancet*, 11/1933, 1081.

[P1-87] **Iodothyroglobulin** may be obtained from fresh thyroid tissue by extraction with normal saline and precipitation by half saturation with ammonium sulphate. The moist precipitate may be purified by redissolving in normal saline, again precipitating by half saturation with ammonium sulphate, dialysing free from salts and finally precipitating from aqueous solution by alcohol. A more rapid procedure is to extract the glands with 0.1 M. sodium acetate and acetic acid.—Barnes, *Proc. Soc. exp. Biol.*, N.Y., 1932, 29, 680.

#### *The Preparation and Properties of Thyroglobulin.*

Pig thyroid extracts of pH 4.8 to 5 deposit in the cold a substance possessing the property of a nucleoprotein. This may be removed and the thyroglobulin can then be precipitated from the neutralised solution by half saturation with  $\text{Na}_2\text{SO}_4$  at 35°. The use of  $\text{CH}_3\text{COOH}$  as a precipitant is not recommended.

**Catechins.** If the "hormones" are to be regarded as stimulating or exciting substances, then the "catechins" are their antagonists, whose special province is to prevent excessive effects.

of hormones or to modify their action. The catechins are present in the human organism: it is known, for instance, that the blood contains an antithyroidal substance, and this has been isolated as an independent substance from the protein of the blood with which it forms a loose combination. This antithyroidal substance has been used with success in severe exophthalmic goitre.—F. Blum, per *J. Amer. med. Ass.*, i/1933, 55.

**Preparation and Properties of an Antithyrotropic Substance.**

An extract of an antithyrotropic substance prepared from horse serum after injection of thyrotropic hormone. The substance obtained does not antagonise action of thyroxine but *does* depress the metabolic rate of normal animals and inhibits the action of the thyrotropic hormone in normal and hypophysectomised rats.—E. M. Anderson and J. B. Collip, *Lancet*, i/1934, 784.

**Antithyroidin "Mœbius" (Merck, Darmstadt; Martindale, London)**

Thyroidectomised sheep's serum. In exophthalmic goitre. By intramuscular injection or in the form of fluid serum or tablets.

**Thyroidectin (Parke, Davis, London).** A powder prepared from the dried blood of thyroidectomised animals, available in capsules. *Dose*.—1 or 2 capsules thrice daily. In Graves' disease. **Thyroidectomised horse serum** is also available for hypodermic or oral use. *Dose*.—Hypodermically, 1 to 2 ml. twice or thrice weekly; orally, 1 to 5 ml. or more thrice daily.

**Tyronorman (Hommel's Hæmatogen and Drug Co., London).** Purified and concentrated thyroid-dil inhibitory substance. Tablets contain 10 anti-thyroid units; 6 tablets equal one daily dose. Graves' disease and thyrotoxicosis.

**HYPERTHYROIDISM.**—1 tablet three times a day, increasing up to 6 or 9 daily and then gradually decreasing, the treatment being continued for from 4 to 6 weeks. During treatment, meat and stimulants avoided, and plenty of carbohydrates, fruit, vegetables, milk and animal fats given. Only failed in 2 cases out of 18.—E. Herzfeld and A. Frieder, *Dtsch. med. Wschr.*, 1933, 84.

Good results reported from use of Tyronorman in Basedow's disease.—E. Baumann, *Münch. med. Wschr.*, 1934, 81, 57.

**LACTATION.**—Fifty patients treated with Tyronorman secreted an average of 6705 ml. more milk during first five days of puerperium than fifty control cases.—H. Küstner, *Dtsch. med. Wschr.*, 1936, 304.

**Parathyroideum (B.P.C.).**

*Dose*.— $\frac{1}{10}$  to  $\frac{1}{10}$  grain (0.003 to 0.006 g.).

The external parathyroid glands of the ox—dried and powdered. Should be free, or almost free, from thyroid and thymus. It does not contain iodine.

The fresh parathyroid glands weigh on an average 0.09 g. and yield from 0.015 to 0.02 g. of desiccated powder, *i.e.*, 1 = 5 of fresh substance.

The parathyroids are small glands which usually occur in close anatomical relationship to the thyroid gland. They are classified into external and internal—terms which relate to embryological development and do not necessarily denote their position in relation to the thyroid gland, although the external glands are usually found outside the capsule of the thyroid. In man the parathyroids are four in number—two in each lobe of the thyroid. The two internal parathyroids may be placed within the capsule of the thyroid in man and in the bovine species. In dogs both internal and external parathyroids are centrally placed within the thyroid. Accessory parathyroids are not uncommon and may occur in various situations in the neck and thorax—not infrequently in the thymus gland.



**Structure.** The parathyroid glands are composed of masses of epithelium cells divided by strands of connective tissue with sinus-like blood-vessels. The typical cell of parathyroid tissue, called the principal cell, is a polyhedral cell with clear, faintly-staining cytoplasm and a large, darkly-staining nucleus. Scattered throughout the tissue are a few larger cells having eosinophil granules in the cytoplasm and a small, centrally placed, deeply-staining nucleus—the oxyphil cells.

**Physiology.** The parathyroids control calcium and phosphorus metabolism; apart from its importance in the formation of bones and teeth the amount of ionised calcium in the blood serum controls the varying irritability of nerves and the contractility of both voluntary and involuntary muscles, and hence it also influences vascular tone. The normal value for the blood-serum calcium is from 9 to 11 mg. of Ca per 100 ml. of blood. The inorganic phosphorus does not normally exceed 5 or 6 mg. per 100 ml. Removal of the parathyroids is followed by tetany and death in a few days, the serum calcium is reduced, there is increased excretion of calcium and nitrogen, increase in the absolute and relative ammonia in the urine, and increase in the ammonia content of the blood. Hyperparathyroidism is characterised by increased viscosity of the blood, and a depletion of calcium from the osseous system. In hypoparathyroidism there is lowered calcium content of the blood and hyperexcitability of nerves and muscles. The occurrence of methylguanidine in the blood after parathyroidectomy may result from the action of phosphoric acid on creatinine and it is possible that in hypoparathyroidism methylguanidine may accumulate in the blood in sufficient amounts to be toxic. A detoxicating action has been stated to be a function of the parathyroid glands, but there is insufficient evidence to confirm or disprove this.

The increase in methylguanidine which occurs in tetany is due to dehydration and seems to bear no relation to the blood-serum calcium—Bryan, Minot and Chastain, *Amer. J. Physiol.*, 1933, 106, 738.

The occurrence of two types of cells in parathyroid tissue has been held to denote that the glands may exert two different functions but it is not yet known which cells produce the hormone which controls parathyroid metabolism and what the other function, if any, may be.

**Uses.** Desiccated parathyroid gland has been given orally in tetany, tetany of pregnancy, tetany of childhood, epilepsy, paralysis agitans, sprue (with calcium lactate) and eclampsia. It is generally held that no increase of blood-serum calcium can be detected after oral administration, and *Extractum Parathyroides* (q.v.) hypodermically is to be preferred.

A serious drawback to parathyroid extract is a gradual loss of its effect: an apparent immunity is established. Its chief use is in the treatment of low-calcium tetany, in which it may be a life-saving measure. It is of use also in conditions in which decalcification of the body is desired, such as abnormal deposits of calcium in the tissues and abnormal storage of metals (lead or radium) in the bone.—J. C. Aub, *J. Amer. med. Ass.*, ii/1936, 197.

**CALCIUM DEFICIENCIES** treated by parathyroid. Varicose ulcer found to improve up to a point under intramuscular injection of calcium salts, but did not proceed to complete cure, and under parathyroid healing was more rapid in cases at rest and in early cases.  $\frac{1}{8}$  gr. of dried gland was given until laboratory tests showed that ionised calcium had returned to normal.—W. R. Groves and I. W. C. Vines, *Brit. med. J.*, 11/1921, 40, 152, 687. See also *Lancet*, 11/1921, 283, *Brit. med. J.*, 1/1922, 791. Leucocyte activity is stimulated.—*ibid.*, 1/1923, 106.

Gastric, duodenal and varicose ulcers well treated —L. Williams, *Brit. med. J.*, 1/1923, 1010.

**OTOSCLEROSIS**.—Parathyroid  $\frac{1}{2}$  or  $\frac{1}{4}$  gr daily, increased to  $1\frac{1}{2}$  or 2 gr. Hearing and general health improved —E. Watson Williams, *Lancet*, 1/1923, 814.

**PAROXYSMAL TACHYCARDIA**—Parathyroid  $\frac{1}{8}$  gr thrice daily used with remarkable effect.—C. Dukes, *Brit. med. J.*, 11/1921, 987.

**PSORIASIS**.— $\frac{1}{8}$  gr. parathyroid daily.—*Brit. med. J.*, 1/1924, 772.

**SPASMODIC RHINORRHOEA**.—Calcium lactate 15 gr and parathyroid  $\frac{1}{16}$  gr twice daily —W. M. Mollison, *Brit. med. J.*, 11/1929, 1052.

**SPRUE**—Parathyroid  $\frac{1}{8}$  gr. twice daily with calcium lactate 10 or 15 gr thrice daily, gave good results —H. Harold Scott, *Lancet*, 11/1923, 876, *Brit. med. J.*, 11/1924, 308. V. Coates, *ibid.*, 623. C. F. Shelton, *Brit. med. J.*, 11/1925, 844.

But there is no statement that the author tried calcium lactate without the parathyroid —Prof. Swale Vincent, *Brit. med. J.*, 11/1925, 1056. Vines says Scott obtained equally good results without calcium at all—using the parathyroid alone —*Brit. med. J.*, 11/1925, 1059.

No conclusive evidence of efficacy in sprue —Dan T. Davies, *Lancet*, 1/1930, 203.

All the older remedies reviewed. Certain cases did well with calcium and parathyroid —Lt.-Col. H. W. Aston, *Brit. med. J.*, 1/1931, 222.

**TETANY**.—Some good results have been reported —Prof. Swale Vincent, *Lancet*, 1/1923, 130.

Tetany following removal of right lobe of thyroid gland benefited from parathyroid  $\frac{1}{8}$  gr hypodermically and large dose of calcium lactate.—Davies, *Brit. med. J.*, 1/1923, 512.

Use of parathyroid in tetany, œdema, epilepsy and jaundice —*Prescriber*, 1928, 165.

Acute parathyroid tetany relieved and controlled without use of parathyroid. The parathyroids do not perform a metabolic function indispensable to life —Drogstedt, per *Prescriber*, 1929, 172.

**Tabellæ Parathyroidel (B.P.C.)**. Contain  $\frac{1}{8}$  gr (0.006 g)

**Ostellin with Parathyroid Tablets (Glaxo Laboratories, London)** Contain 500 i.u. of vitamin D (calciferol),  $\frac{1}{8}$  gr desiccated parathyroid, and 2 gr. calcium glycerophosphate. Dose —3 to 6 tablets daily.

[P1-57] **Thyrocalx (Sharp & Dohme, London)** Tablets containing desiccated thyroid  $\frac{1}{2}$  gr, desiccated parathyroid  $\frac{1}{8}$  gr, calcium lactate 5 gr. For use in calcium deficiencies.

**Extractum Parathyroidel (B.P.C.)**.

**Dose**.—20 to 40 units, a unit being one-hundredth of the amount required to raise the blood-calcium of a 20 kg. dog by 5 mg. per 100 ml.

Prepared by extracting parathyroid glands with 5% hydrochloric acid at 100°; after cooling, fat is removed and sodium hydroxide added to pH 8, hydrochloric acid is added to precipitate protein (maximum precipitation occurs at about pH 5.5). The precipitate is removed, redissolved in NaOH and proteins again precipitated by hydrochloric acid. After this process has been repeated several times the filtrates are mixed and contain the active principle of the glands.

For details of method of preparation, see J. B. Collip, *J. biol. Chem.* 1925, 63, 395; *J. Amer. med. Ass.*, i/1927, 565. Also J. B. Collip and E. P. Clark, *J. biol. Chem.*, 1925, 66, 133, and 1925, 63, 439.

For methods of biological assay, see Vol. II. See also F. J. Dyer, *Quart. J. Pharm.*, 1935, 513.

**Liquor Parathyroidi (U.S.P. XI).** *Average dose.*—25 units, by hypodermic injection. One millilitre contains 80 to 120 parathyroid units, each unit being one-hundredth of the quantity required to raise the calcium level of 100 ml. of dog's blood serum by 0.001 g. within 16 to 18 hours after administration.

**Uses.** The effects produced by injection of a solution of the parathyroid hormone are (a) increase in the amount of calcium and decrease of phosphorus in the blood; (b) increase in the Ca and P excretion in urine. The calcium is obtained chiefly from the bones. Overdosage may cause kidney damage, rise in blood pressure and accumulation of nitrogenous waste products in the tissues; deposits of calcium may occur in the soft tissues and calculi form in the kidney.

The rise in blood calcium following intramuscular injection of the hormone occurs after a latent period of a few hours and persists for about 20 hours. After a few months' treatment, tolerance seems to be established and the effect diminishes.

It is doubtful if parathyroid hormone increases the amount of calcium salts absorbed from the intestine, and in this respect its action differs from that of vitamin D, which increases the serum calcium by increasing absorption from the intestine and the effect may last as long as two weeks after administration has ceased.

In normal subjects parathyroid extract lowers the glycaemia during fasting and increases carbohydrate tolerance, its action being very similar to that of insulin. In ten cases of diabetes intramuscular injection of one millilitre of the extract produced a clear hypoglycaemic effect, slightly lower than that produced by insulin. Administered along with insulin it may increase the hypoglycaemic action of the insulin, or it may scarcely modify it or even slightly inhibit it, given alone parathyroid extract has an undoubted insulin-like action.—A. Ferrannini, *Policlinico*, 1935, 366.

**OSTEITIS DEFORMANS** in a woman aged 54 much improved by 5 to 10 units of Parathormone daily for two years with periods of intermission. The serum calcium was normal and 30 gr. of sodium acid phosphate were given daily to decrease absorption of calcium and increase excretion in urine—G. H. Colt and A. Lyall, *Brit. med. J.*, ii/1933, 10.

**POST-OPERATIVE TETANY** treated with 5 to 10% solution of calcium chloride by slow intravenous injection in doses of 10 ml., and high calcium diet. If spasms recur 10 to 50 units daily of Parathormone are helpful but it is too slow for use in emergency.—R. F. Farquharson, *Canad. med. Ass. J.*, 1933, 629.

**TETANY.**—The treatment of infantile tetany by Parathormone is a profound mistake. Although Parathormone bears a superficial resemblance to vitamin D in its effect in raising the blood calcium, Parathormone, so far from having a vitamin D-like effect does not influence calcium or phosphate absorption in rickety conditions, but has, in fact, a definitely deleterious action, aggravating the underlying error, draining still further minerals from the impoverished bones and causing a net loss to the body as a whole. Vitamin D is the proper remedy for infantile tetany.—L. J. Harris, *Brit. med. J.*, ii/1933, 372.

While Collip's Parathormone is active in raising the level of the serum calcium and relieving the symptom of parathyroid tetany it is not satisfactory unless injected in large and repeated doses. It is also expensive. In most cases, therefore, it is impracticable to employ it. Calcium chloride (q.v.) intravenously or *per os* is an excellent emergency measure.—D. Campbell, *Lancet*, i/1935, 869.

**RADIUM POISONING.**—Parathyroid extract and a low calcium diet slightly increased radium elimination in three cases—Craven and Schleendt, *J Amer med. Ass.*, 1/1935, 959.

**Euparatorone** (*Allen & Hanburys, London*) Biologically standardised solution of parathyroid hormone, 20 units per ml. *Dose*—In adult tetany, 20 to 60 units daily in 8-hourly doses may be necessary; in infantile tetany, 10 to 20 units daily may suffice. In other conditions, 10 to 20 units daily or every second day.

**Parathormone** (*Lilly, London*) A solution of the active principles of the parathyroid glands. Is standardised on the relationship between the dose given and the increase in blood-serum calcium, the unit of potency being 0.01 of the amount of extract that produces an average rise of 5 mg. in blood-serum calcium in a 20-kilo dog in 15 hours. *Dose*.—Varies with individuals and conditions. Infantile tetany may be relieved by 10 to 20 units a day, but repeated serum determinations should be made to estimate the reactions. In tetany daily doses of 20 to 60 units are used. It is usually given subcutaneously though it may also be given intramuscularly or intravenously. Calcium gluconate or calcium lactate in large doses *per os* should accompany its use. Excessive dosage leads to increased concentration of calcium and phosphate in the blood, and their increased excretion.

**Paroldin** (*Parke, Davis, London*). Parathyroid extract standardised on its ability to raise the blood-serum calcium of normal dogs. It is supplied in solution containing 100 units per ml, the unit being one-hundredth of the amount necessary to raise the blood-serum calcium by 1 mg. per 100 ml. *Dose*.—20 to 40 units subcutaneously or intramuscularly.

**An Anti-Growth Principle** from parathyroid glands. Parathyroid glands extracted with a mixture of a fat solvent (e.g., acetone, benzene or toluene) and dilute acid (e.g., sulphuric or hydrochloric), the fat solvent removed and the acid solution brought to pH about 4.8. The insoluble matter is filtered off after standing, the filtrate when concentrated inhibits tissue growth but does not produce hypercalcaemia.—N. Evers, C. J. Eastland and J. H. Thompson *Biochem. J.*, 1932, 26, 2123

## TRAGACANTHA

*B.P., U.S.P. XI, P. Helv. V, P. Dan.*

From *Astragalus gummifer* and some other species (*Leguminosæ*).

**Uses.** Tragacanth mucilage answers well for suspending Tinct. Jalapæ, Liquor Quininae Ammoniatæ, Tinct. Cannabis and Tinct. Myrrhæ, but is useless for Tinct. Benzoini Co. and Tinct. Tolu. For these a mixture of mucilage of tragacanth and mucilage of acacia is best. In the case of a mixture containing 1 dr. of resinous tincture to the ounce, dilute 1 dr. of mucilage of acacia with as much water as possible, add the tincture, and lastly add the mucilage of tragacanth. For other resinous tinctures mucilage of acacia alone yields satisfactory mixtures. The mucilage is best diluted with as much water as possible, and the tincture then added.

Tinctura Hydrastis, which in absence of salts requires no suspending agent, should have an addition of mucilage of tragacanth if salts are present. Tinctura Lupuli and Tinctura Cimicifugæ require no addition either in presence or absence of salts.

Tinctura Podophylli requires no suspending agent in the absence of salts, but if any are present mucilage of acacia is best used.

**Cremor Emolliens** (*U.C.H.*) *Syn.* SKIN CREAM.

Tragacanth 1, methylated spirit 7, glycerin 14, olive oil 3½, simple tincture of benzoin 2, water to 100

**Gelanthum** (*P.E.H.C.*) Tragacanth 110 gr., acacia 30 gr., gelatin 120 gr., water 10 oz.; mix, heat, filter and add glycerin 6 dr., thymol ¼ gr., water to 12 fl. oz. A basis for various applications for skin medication.

**Glycerinum Tragacanthæ** (*B.P.C.*). 1 in 5½. A pill excipient; must be used sparingly.

**Lotio Tragacanthæ** (*B.P.C.*) *Syn.* LOTIO EMOLLIENS

Tragacanth 0.5% *w/v* with spirit of chloroform, tincture of tolu, Cologne spirit, glycerin and water.

**Mucilago Tragacanthæ** (*B.P.*).

*Dose*—1 drachm to 1 ounce (4 to 30 ml.) or more.

Tragacanth 1½% *w/v* with alcohol 2½% *v/v* in chloroform water

Mucilage made from whole gum has a much higher viscosity than that made from powdered gum and, if not heated, increases in viscosity on keeping. There is no advantage in adopting any particular method of preparation when the mucilage is to be diluted and used for its power of suspending an insoluble powder.—H. Brindle and H. Burlinson, *Quart J Pharm*, 1934, 492. See also G. Middleton, *ibid.*, 1936, No. 3.

**Mucilago Tragacanthæ** (*U.S.P. XI*)

Tragacanth 6% *w/w* and glycerin 18% *w/w*, in water.

**Pasta Tragacanthæ Composita** (*B.P.C.*)

*Syn.* PASTA

LUBRICANS, CATHETER LUBRICANT.

Tragacanth 1% *w/v* with boric acid, glycerin, oil of lavender and decoction of chondrus

[P1] **Catheter Lubricant** (*Meltzer's Formula*) Triturate tragacanth 3 with glycerin 20, add water 100, sterilise, and add mercury oxycyanide 0.25

**Pulvis Tragacanthæ Compositus** (*B.P.*).

*Dose*.—10 to 60 grains (0.6 to 4 g.)

Tragacanth 15%, with acacia, starch, and sucrose. Is used as a suspending agent, 10 gr. to 1 oz. Specially useful for bismuth oxynitrate.

**Ceratonis Gummi.** *Syn. and Prop. Name.* CAROB GUM, LUCTIN (*Anglo-Gummiferous Co., London*)

The separated endosperms of the seeds of the locust bean tree, *Ceratonia siliqua*. A substitute for tragacanth

**Mucilago Ceratonis.** Carob gum 1 g, glycerin 3 ml, benzoic acid 0.15 g, triturate and add water to 80 ml., heat the mixture on a water-bath for 30 minutes

Various other formulæ given for carob gum preparations.—W. A. Knight and M. W. Dowsett, *Pharm J*, 1/1936, 35. The mucilage may be prepared without the use of glycerin.

## TRINITROPHENOL

*B.P., U.S.P. XI, P. Jap., Fr. Cx., P. Ital V, F.E. VIII, P. Helv. V.*

$C_6H_3(OH)(NO_2)_3[OH : (NO_2)_3 = 1 : 2 : 4.6] = 229.0.$

*Syn.* ACIDUM PICRICUM, PICRIC ACID, CARBAZOTIC ACID.

[P1] "*Picric acid.*"

[B3] "*Picric acid—in substances containing less than 5% of picric acid.*"

**Dose.**—1 to 5 grains (0.06 to 0.3 g.).

Is formed by cautiously adding phenol to fuming nitric acid, heating the mixture, and purifying by re-crystallisation. It is in yellow, shining, bitter-tasting crystals, which melt at  $121^{\circ}$  to  $123^{\circ}$ —the yellow liquid may be distilled without decomposition. Heated rapidly to  $300^{\circ}$  in the open, it burns.

**Soluble** 1 in 90 of water with yellow colour, 1 in 10 of alcohol 90%, and about 1 in 20 of ether.

**Antidotes.** Empty stomach by stomach tube, washing out thoroughly with plenty of water. Give raw white of egg and milk freely. Purgative dose of sodium sulphate. Saline infusion.

**Uses.** Solutions or ointment are applied in the treatment of burns, erysipelas, pruritus, eczema, chilblains and gonorrhœa. Local use in skin affections may cause dermatitis. In stomatitis mercurialis a watery paste of the compound has been applied every 2 days—relieves pain and removes ulceration. Papillary erosions of the cervix uteri have been treated by swabbing with saturated alcoholic solution for 3 minutes twice or thrice weekly.

Vaccinated surfaces may be treated by painting with a 4% alcoholic solution 48 hours after insertion of the lymph; the application lessens the degree of reaction. Trinitrophenol is stated to be about 4 times as efficient as phenol as a local antiseptic.

**Carbasus Trinitrophenolis (B.P.C.).** *Syn.* PICRIC GAUZE 2%. Wool impregnated with trinitrophenol is also prepared.

[P1] **Liquor Trinitrophenolis (B.P.C.).** *Syn.* LIQUOR ACIDI PICRICI. 5% w/v in alcohol.

**Lotio Trinitrophenolis (B.P.C.)** *Syn.* LOTIO ACIDI PICRICI. 1% in water. May be diluted with 1 or more parts of water, as required.

A useful first-aid application for burns. May be applied on lint or gauze. After 48 hours remove and wash with potassium permanganate 5 gr. in water 16 oz.

Washing with weak ammonia and then with hydrogen peroxide removes the stains.

For burns not advised. Permanently scarred faces in the Jutland Battle—C. P. G. Wakely, *Med. Pr.*, ii/1929, 32.

GONORRHOEA treated by 1 in 400 to 1 in 200 solution. An extremely potent germicide, and good when tolerated.—D. Lees, *Brit. med. J.*, ii/1921, 480.

**Pigmentum Trinitrophenolis et Camphoræ.** *Syn.* PIGMENTUM ACIDI PICRICI ET CAMPHORÆ. Trinitrophenol 2, camphor 50, and alcohol 90% to 100. Ringworm has been treated by painting this over the scalp twice daily, the hair being clipped close and the scalp washed once or twice a week and covered by a calico cap. Generally the ringworm hairs are loosened, and come away with their bulbous portions in from 10 to 30 days. The paint is inflammable.

**Unguentum Trinitrophenolis (B.P.C.).** *Syn.* UNGUENTUM ACIDI PICRICI.

2%. For pruritus of scrotum and gonorrhœa. Also for burns; it relieves pain, and may be left 48 hours without changing. For burns of the eye it is preferred by some to solution, using a little cocaine solution beforehand.

**Ammonii Picras.**  $C_6H_5(NO_2)_2O \cdot NH_4 = 246$  1.

*Dose.*— $\frac{1}{2}$  to 1 grain (0.01 to 0.02 g.) in solution.

Yellow crystals exploding if rapidly heated in a test tube, but without loud detonation.

*Soluble* 1 in 100 of water, 1 in 85 of alcohol.

*Uses.* This and the potassium salt have been thought to act like quinine; malaria has been treated by ammonium picrate in India. They are also used for hardening tissues prior to microscopic examination and as a urine test for albumin.

**Mistura Ammonii Picratis.**

*Dose.*— $\frac{1}{2}$  ounce (15 ml.) thrice daily.

Saturated ammonium picrate solution 30 m., syrup of orange  $\frac{1}{2}$  dr, water to  $\frac{1}{2}$  oz. As a bitter tonic in convalescence.

## TROCHISCI

Lozenges consist of sugar bases containing gum, which causes the mass to set hard on drying. The medicaments in lozenges are usually those having a local action on the throat, but in some cases, such as sulphur and bismuth lozenges, they afford a convenient method of giving the drugs. The following are the usual bases employed and the lozenges made from them.

**GENERAL BASIS.** This is the official basis for lozenges in the *British Pharmacopœia*, and consists of a simple basis flavoured with tincture of tolu. Tannic acid, extract of krameria, krameria and cocaine, morphine, morphine and ipecacuanha.

**FRUIT BASIS.** A basis flavoured with black currant. Benzoic acid, compound ammonium chloride, catechu, guaracum resin, eucalyptus.

**ROSE BASIS.** A basis flavoured with oil of rose Potassium chlorate, compound bismuth.

**SIMPLE BASIS.** An unflavoured basis. Antacid, reduced iron, liquorice (Brompton cough lozenge), ipecacuanha, santonin.

(For composition and uses of various B.P., B.P.C., and other lozenges, see under the drug.)

## UREA

B.P.C.

$CO(NH_2)_2 = 60.05$ .

*Syn.* CARBAMIDE.

*Dose.*—15 to 240 grains (1 to 16 g.) thrice daily. May be given in a mixture flavoured with lemon syrup. Larger doses are frequently given. Hypodermically, a 1 in 6 solution has been given, but it is seldom used in this way.

Colourless crystals with cooling, saline taste. M.p.  $130^\circ$  to  $132^\circ$

*Soluble* 1 in 1 of water, 1 in 5 of alcohol 90%; 1 in 1 of boiling alcohol 90%; insoluble in ether and in chloroform.

*Uses.* Urea has diuretic properties and is given to some extent in gout and kidney disease. In the past it was given in phthisis.

It has marked bactericidal properties and has been suggested for wounds. It is mainly given as a test of renal efficiency.

(For technique of urea concentration test, see Vol. II, 20th Edn., p. 329.)

**CEDEMA.** Grave genuine nephrosis (nephritis with cedema, without hypertension or hæmaturia). Complete recovery under treatment with urea up to 100 g. daily.—*Per J. Amer. med. Ass.*, ii/1925, 2058.

A useful diuretic in doses of 30 to 60 g. a day in a small amount of water after meals in cases of heart failure with cedema.—*Per J. Amer. med. Ass.*, ii/1925, 1753. *See also Brit. med. J. Epit.*, i/1926, 2.

After ingestion of 100 g. of urea by normal persons the urea-nitrogen of the blood can be raised to a figure comparable with that obtained in chronic nephritis. When blood urea exceeds 70 mg. per 100 ml., headache, dizziness and somnolence may occur. It can be given over long periods and has been administered in doses above mentioned in advanced cardiac decomposition. With continuous administration, daily urine volume can be maintained at almost constant level. Its use as a diuretic deserves greater popularity.—*J. Amer. med. Ass.*, ii/1925, 2036.

Epstein's advice that patients suffering from marked cedema or ascites resulting from parenchymatous nephritis should receive liberal protein diet is substantiated. Large doses of urea given in such cases resulted in disappearance of the dropsy. 30 g. or more *per diem* persevered with. Bad cases have been cured. In interstitial cases where nitrogen retention is more or less well marked, protein, especially meat, is on the whole contraindicated. Milder cases are, however, probably not benefited by strict dietetic limitations. The whole question of protein diet in kidney disease requires much investigation.—H. MacLean and A. E. Russell, *Lancet*, i/1920, 1305, and *Lancet*, i/1925, 1213, *Practitioner*, i/1926, 67.

**OTITIS MEDIA** 20 cases of purulent otitis media were treated by drops of a saturated solution of urea 4-hourly, after washing out the meatus with normal saline. The discharge lost its foul odour in a few hours. Some cases cleared up in 36 hours, but the usual time taken was 3 to 6 days.—J. Foulger and L. Foshay, *J. Lab. clin. Med.*, 1935, 1113.

**SCAR TISSUE** Best results of softening of, obtained by injection under non-adherent scars of a concentrated solution of urea. Care necessary as necrosis caused when injected under an adherent scar.—*Per Practitioner*, i/1926, 332.

**Hauftus Urea (C.X.H.)** Urea 15 g., syrup of orange 15 ml., water to 100 ml.

**Hauftus Urea Composita (K.C.H.).** Urea 4½ dr., tincture of orange 15 m., water to 3½ oz. Both the above are given for the urea concentration test.

**Urethanum (B.P.C., P. Helv. V).**  $\text{CO}(\text{NH}_2)\text{OC}_2\text{H}_5 = 89.06$ . *Syn.* ETHYL CARBAMATE (*Fr. Cx.*, *P. Dan.*, *F.E. VIII*, *P. Ital. V*).

**Dose.**—½ to 1 drachm (1 to 2 g.). Tablets, 5 grains (0.3 g.). Colourless, odourless crystals with saline taste. M.p. 47.5° to 50°, b.p. about 180°.

**Incompatible** with caustic alkalis and with acids.

**Soluble** 1 in 2 of water, 1 in 1 of alcohol 90%, and in ether, chloroform, glycerin and oils.

**Uses.** Mild hypnotic with very low toxicity. Produces normal sleep without after-effects or depressant action on the heart, and is especially suitable for children, the aged, and those with heart affections. Is sometimes useful in delirium tremens and in acute mania, but large doses (½ to 1 drachm) are necessary, and more powerful hypnotics are preferred.

(*For Quinine and Urethane, see p. 820.*)

**Bromoisovalerylanylurea (P.G. VI, P. Ned. V, P. Svec. X, P. Dan.).**  $(\text{CH}_3)_2\text{CH}\cdot\text{CHBr}\cdot\text{CONH}\cdot\text{CONH}_2 = 223.0$ . *Syn. and Prop. Names.* BROMISOVALUM (*P. Helv. V*), BROMISOVALERYLUREA (*F.E. VIII*), α-MONOBROMISOVALERYLUREA, BROMURAL (*Knoll, Ludwigshafen; Pharmaceutical Products, London*), DORMIGENE (*Allen & Hanburys, London*).



**Dose.**—5 to 10 grains (0.3 to 0.6 g.). *P. Helv. V* has max. single dose 15 grains, max. in 24 hours 30 grains approx.

White, crystalline powder with slightly bitter taste. M.p. 145° to 150°.

**Soluble** 1 in about 450 of water; readily soluble in alcohol and ether.

**Uses.** Hypnotic, inducing sleep in from 5 to 25 minutes after ingestion. The effect lasts from 4 to 5 hours, and may be followed by natural sleep.

**Elbon-Ciba** (*Ciba, London*). Cinnamoyl-*p*-oxyphenylurea,  $C_6H_5 \cdot CH : CH \cdot CO \cdot OC_6H_4 \cdot NH \cdot CO \cdot NH_2 = 282$ , in 0.5 g tablets

**Dose.**—In tuberculosis 1 tablet every 3 hours (8 per 24 hours), increased if no response, then decreased. In hay-fever, prophylactically 1 tablet twice a day, increased during hay-fever season to 2.

Stated to have antipyretic and antiseptic action. Used in pulmonary tuberculosis, for infectious catarrhs of respiratory tract, and in chronic endocarditis, also for hay-fever and asthma.

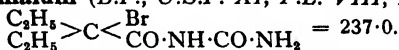
**ASTHMA.** Relief in long-standing cases—30 to 60 grains a day—*Brit med J.*, 1/1925, 641.

**Iodival** (*Knoll, Ludwigshafen; Pharmaceutical Products, London*).  $\alpha$ -Mono-iodoisovaleryl urea. A sedative iodine compound, containing not less than 40% I, in powder or 5-gr. tablets. **Dose.**—5 grains thrice daily. A sedative substitute for inorganic iodides

**Neodorm** (*Knoll, London, Pharmaceutical Products, London*)  $\alpha$ -isoPropyl- $\alpha$ -bromobutyramide **Dose**—3 tablets daily. For insomnia

[P1 81 84] **Somnosol** (*Napp, London*)  $\alpha$ -Bromoisovalerylurea 5 gr, amido-pyrene 2½ gr **Dose**—Sedative, 1 to 3 tablets thrice daily; soporific, 1 to 3 tablets with a hot drink.

**Carbromalum** (*B.P., U.S.P. XI, F.E. VIII, P. Dan.*).



**Syn. and Prop. Names.** URADAL,  $\alpha$ -BROMO- $\alpha$ -ETHYLBUTYRYL-CARBAMIDE, BROMODIETHYLACETYLUREA, BROMDIÆTHYLACETYL-CARBAMIDUM (*P. Belg. IV, P. Svec. X*), BROMADALUM (*P. Helv. V*), DIÆTHYLOBROMOACETYLUREUM (*P. Ned. V*), ADALIN (*Bayer Products, London*) (*P.G. VI*), NYCTAL (*Sitsa, Paris; Roberts, London*), PLANADALIN (*Pharmaceutical Specialties (May & Baker) Ltd., London*).

**Dose.**—5 to 15 grains (0.3 to 1 g.). *U.S.P. XI* average dose 8 grains. *P. Helv. V* gives max. single dose 23 grains, max. in 24 hours 45 grains approx. As a hypnotic, should be given half an hour before bedtime and followed by a hot drink.

Tasteless, crystalline powder. M.p. 116° to 118°.

**Soluble** 1 in about 3000 of water, 1 in 18 of alcohol 95%, 1 in 14 of ether, 1 in 3 of chloroform; slightly soluble in light petroleum. It is also soluble in strong mineral acids and in caustic alkali solutions. The above (*B.P.*) solubility figures are identical with those of *U.S.P. XI*, which are obtained at 25°.

**Uses.** A safe hypnotic of medium strength. Does not produce after-effects. Is useful in insomnia due to worry, overwork or excitement, but is less efficient in insomnia due to pain.

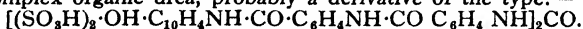
[P1 81 87] **Sedormid** (*Hoffmann-La Roche, London*). Allylisopropylacetylurea in 4-gr. tablets. **Dose.**—As sedative, ½ to 1 tablet 2 or 3 times a day. As hypnotic, 1 or 2 tablets (or more) 20 minutes before retiring. Its activity is stated to be

midway between that of the barbiturates and of the bromides or valerian. It is rapidly eliminated, thus avoiding accumulation. A sedative for nervous insomnia, Graves' disease, disturbances of menstruation and the climacteric, before operation and as an aid to drug-withdrawal treatment.

### Symmetrical Ureas and Related Compounds.

**Antrypol** (*British Drug Houses, London*). Symmetrical urea of sodium-*m*-aminobenzoyl-*m*-amino-*p*-methylbenzoyl-1-naphthyl-amino-4 : 6 : 8-trisulphonate. Administered intravenously in isotonic saline in the treatment of trypanosomiasis.

**Germanin** (*Bayer Products, London*). *Syn.* BAYER "205." A complex organic urea, probably a derivative of the type:—



*Dose.*—The injection is made intravenously in doses of 1 g. in 10 ml. of water at a time, but may also be given subcutaneously. A white powder soluble in water.

Used in the treatment of trypanosomiasis.

The best effect seemed to be obtained by giving 3 injections at close intervals, and spacing out the remainder into 1 g. doses once a week. The effects on the kidneys need not be regarded as contraindicating its use.—P. Manson-Bahr. Records of 9 cases of trypanosomiasis in Europeans treated with Bayer "205."—G. C. Low, *Brit. med. J.*, 1/1923, 149.

As much as 5 g. have been given intravenously in 50 hours to a native.—N. H. Dyce Sharp, *Lancet*, 1/1923, 1026.

If given in smaller doses than 1 to 1.5 g. the organisms may lose their susceptibility to the drug.—*Brit. med. J.*, 1/1923, 36. See also J. W. Stephens and Warrington Yorke, *J. trop. Med. (Hyg.)*, 1923, 65, *Lancet*, 1/1926, 427.

Bayer "205" and Atoxyl do not cure trypanosomiasis when it has reached the second stage. 0.05 g. intraspinally may cause grave accidents and 0.3 g. mortal accidents. Cutaneous eruption noticed and renal irritation sometimes ending in nephritis.—Per *J. trop. Med. (Hyg.)*, 1925, 36.

Cannot be considered a cure for late cases. Tryparsamide almost equal and easier to work.—A. T. Schofield, *Brit. med. J.*, 1/1926, 92.

It may be better for *T. rhodesiense* than for *T. gambiense*. Of value where trypanosomes become fast to arsenic or antimony.—P. Manson-Bahr, *Lancet*, 1/1927, 132.

Though Bayer "205" caused rapid disappearance of the trypanosomes, the nephritis, and in some cases amblyopia progressing to complete amaurosis, militated against its general employment.—Work of Sleeping Sickness Commission in Portuguese W. Africa in 1923, per *Trop. Dis. Bull.*, 1928, 784.

A dose of 2.0 g. of Bayer "205" administered to an adult may be expected to confer protection against *T. gambiense* and *T. rhodesiense* for at least 3 months. The protection may last much longer.—H. L. Duke, *Lancet*, 1/1936, 469.

**Moranyl.** *Syn.* FOURNEAU 309 (*Société Parisienne d'Expansion Chimique, Paris*). The symmetrical urea of disodium *m*-aminobenzoyl-*m*-amino-*p*-methylbenzoyl-1-naphthylamino-4 : 6 : 8-trisulphonate.

Administered in trypanosomiasis as a 10% aqueous solution in doses up to 10 ml. by subcutaneous or intravenous injection.

"No. 309" like "205" proved inferior to arsenicals. Peripheral sterilisation easily obtained but of short duration. Causes albuminuria in most cases. Preventive action good prophylactic action in man not yet proved.—Per *J. trop. Med. (Hyg.)*, 1926, 344.

**Prontosil** (*Bayer Products, London*). *Syn.* SEPTOSON.

The hydrochloride of 4'-sulphamido-2 : 4-diaminoazobenzene, a red, crystalline powder soluble 1 in 400 of water, issued in 0.3-g. tablets for oral administration. This is the original product. It is now replaced by PRONTOSIL ALBUM. (*See p.* 910.)

**Prontosil Album** is *p*-aminophenylsulphonamide. It is a colourless, non-staining compound which is chemically simpler, cheaper, and probably better tolerated than the original red Prontosil. Is issued in 0.3 g. tablets for oral administration.

**Prontosil S** (*syn.* PRONTOSIL SOLUBILE) is the disodium salt of 4'-sulphonaminophenylazo-1-hydroxy-7-acetylaminonaphthalene-3 : 6-disulphonic acid. It is soluble 1 in 25 of water, and is issued in ampoules containing 5 ml or 10 ml. of 2.5% solution for intramuscular injection.

*Dose.*—20 to 40 ml. (up to 60 or even 90 ml. occasionally) per day of the solution intramuscularly in two or three doses and 3 to 6 tablets of Prontosil Album daily *per os*. The amount given by injection is reduced as the clinical condition of the patient improves. Treatment may be continued for from 3 to 16 days.

It has been given intravenously but severe malaise and nausea may be produced. Owing to ready solubility rapid absorption takes place from intramuscular injection, and intravenous administration is therefore rarely necessary.

*Uses.* Chemotherapeutic agent for all streptococcal infections, especially those due to *S. pyogenes*. Has been used with success in puerperal sepsis, erysipelas, scarlet fever, streptococcal inflammation of the throat and streptococcal arthritis.

Makers' warning re intravenous administration.—*Lancet*, 11/1936, 107.

Prontosil is the first drug that has been shown to have a specific and regular effect on an acute bacterial infection, when administered by mouth.—*Lancet*, 1/1936, 1303.

Prontosil is extremely harmless, rabbits and mice tolerate at least 500 mg per kilo body weight by mouth and subcutaneously. It is pharmacologically an extraordinarily negative compound which displays an almost selective chemotherapeutic action in the streptococcal sepsis of mice, though it has no particular action on the streptococcus in experiments *in vitro*.—H Hörlein, *Proc. R. Soc. Med.*, 1936, 321.

In 38 puerperal fever cases infected by hæmolytic streptococci treated by oral plus intravenous or intramuscular injections of Prontosil, the impression has been gained that in many of the more severe cases the drug has exerted a definitely beneficial effect manifested by unexpectedly prompt fall of temperature and remission of symptoms, with a substantial reduction in the case-mortality of the whole series. Three patients in whom there was judged to be a generalising peritonitis on admission recovered without laparotomy under very large doses of the drug. Further clinical trial is amply justified, and there is more hope of controlling these streptococcal infections by the early administration of this or some related chemotherapeutic agent than by any other means at present available. While the drug has been well tolerated by most of the patients, there have been transient toxic effects in some cases, and many have shown indications of a mildly irritant effect upon the tissues of the urinary tract. Three cases have developed sulphæmoglobinæmia. There is at present no indication from animal experiments that the drug is likely to have a beneficial effect upon puerperal infections by organisms other than the hæmolytic streptococci, and in view of the toxic effects referred to above its administration should be confined to such cases.—L. Colebrook and M. Kenny, *Lancet*, 1/1936, 1286.

*p*-Aminobenzenesulphonamide will protect mice against streptococcal infection. It has the same therapeutic activity as Prontosil but is less toxic when given by mouth, so that it is possible to obtain better protection by giving larger doses. Protection can be obtained against streptococci belonging to different serological types. Some protection of mice against meningococcal infection has been demonstrated, but it has not been possible to demonstrate protection against staphylococci or pneumococci. Increase to three in the number of sulphonamide groups attached to the benzene nucleus is accompanied, not by

increase, but by extinction of the streptococcicidal activity. The anilide of sulphanilic acid is as active as the amide. Sulphanilic acid itself has a smaller, but not negligible, protective action. Azo-compounds derived from *p*-aminobenzenesulphonamide and phenolic cinchona alkaloids are inferior to Prontosil in this respect.—G. A. H. Buttle, W. H. Gray and D. Stephenson, *Lancet*, i/1936, 1290.

**Colsulanyde** (*Crookes Laboratories, London*). Preparations of *p*-aminobenzenesulphonamide for use in streptococcal infections. *Dose*.—45 to 90 grains (3 to 6 g.) per day in three or four doses. Available as a suspension containing  $7\frac{1}{2}$  gr. per drachm, in powders containing  $7\frac{1}{2}$  gr., and in capsules containing  $3\frac{1}{2}$  gr.

**Proseptasine** (*Pharmaceutical Specialities (May & Baker) Ltd., London*). *Syn.* "M & B 125." Benzylaminobenzenesulphonamide,  $C_6H_4(NH_2 \cdot SO_2)NH \cdot CH_2 \cdot C_6H_5$ , issued in 0.5-g. tablets. Administered orally in the treatment of streptococcal infections.

*Dose*.—2 tablets thrice daily for several days. The toxicity is negligible and larger doses may be given with safety.

**S.U.M. 36** (*British Drug Houses, London*). Sterile isotonic solution of the symmetrical urea of *m*-benzoyl-*m*-aminobenzoylamino-naphthol-3 : 6-sodium sulphonate. Solutions contain either 0.002 or 0.01 g. per ml.

*Dose*.— $\frac{1}{10}$  to  $\frac{1}{2}$  grain (0.002 to 0.01 g.) intramuscularly every 5th day on two or three occasions.

In the treatment of gonococcal infections, such as urethritis, vulvitis and ophthalmia; also in very acute cases of gonococcal arthritis.

**S.U.P. 36** (*British Drug Houses, London*). The symmetrical urea of *p*-benzoyl-*p*-amino-benzoyl-1-amino-8-naphthol-3:6-sodium sulphonate.

*Dose*.— $\frac{1}{2}$  to  $\frac{1}{4}$  grain (0.005 to 0.02 g.) intravenously or intramuscularly. Ampoules contain 0.01 g. in 1 ml. Also issued in bulk, 0.1 g. in 10 ml.

In acute staphylococcal infections, in non-metallic intoxications, in pulmonary thrombosis and œdema, venous thrombosis and the pernicious vomiting of pregnancy. Its action is thought to depend on "liberation of + charged and conductor-functioning sodium atoms" from the 6-positions. In the treatment of colds in the head, hay-fever, influenza, acute asthma and other inflammatory conditions of the lungs, also in measles, particularly for the prevention of complications.

In acute pleurisy, bronchitis, broncho-pneumonia and pneumonia (pneumococcal), 0.01 g. should be given on two successive days, and a third dose a few days later if necessary.

**URETHRITIS.** Fever reduced by injections.—F. Kidd, *Lancet*, i/1929, 1094.

**ASTHMA.** Patients with occasional attacks should be treated by S.U.P. 36.—J. E. R. McDonagh, *Lancet*, ii/1929, 271.

**INFLUENZA.** Of value in influenza; 0.5 ml. (= 0.005 g.) into the gluteus medius muscle, followed by 0.75 ml. 4 days later if necessary.—R. M. Pearce, *Brit. med. J.*, ii/1929, 663.

**Influenza.** No benefit noted in 50 consecutive cases.—A. H. Douthwaite, *Brit. med. J.*, ii/1929, 739.

**SEPTIC CONDITIONS**, e.g., boils, quinsy, etc. Not superior to other remedies, but invaluable in catarrhal fever.—W. T. Brown, *Brit. med. J.*, ii/1929, 785.

**S.U.M. 468** (*British Drug Houses, London*) is the symmetrical urea of *m*-benzoyl-*m*-amino-benzoyl-1-naphthylamine-4:6:8-sodium sulphonate.

In malaria, piroplasmosis of horses, and trypanosomiasis of dogs. Fourneau's "No. 309" is allied—J. E. R. McDonagh, *Brit. med. J.*, i/1925, 654, i/1926, 693.

**S.U.P. 468** is the *para* compound corresponding to the preceding.

*Dose*.—0.001 to 0.003 g. intramuscularly. In septicæmia.

## VALERIANA

*B.P., U.S.P. XI, P. Helv. V, P. Dan.*

*Dose*.—5 to 15 grains (0.3 to 1 g.). *U.S.P. XI* average dose 12 grains

The dried rhizome and roots of *Valeriana officinalis* (*Valerianaceæ*), collected in the autumn.

The odour may be removed from a scale pan or from the hands by rubbing with sodium bicarbonate—R. G. Morrison, *Pharm. J.*, i/1935, 106

**Uses.** Given in hysterical and neurotic conditions as a sedative. Its action has been attributed to its unpleasant smell

**Alcoolature Stabilisée de Valériane** (*Fr. Cx. Supp* 1926). Made by adding the fresh entire roots to an equal weight of 95% alcohol while maintained boiling on the water-bath for 20 minutes, allowing to cool and repeating the process, finally making up any loss.

**Elixir Valerianæ** (*B.P.C.*)

*Dose*.— $\frac{1}{2}$  to 2 drachms (2 to 8 ml.) Simple tincture of valerian, 1 in 3, with extract of liquorice and aromatic elixir

[P1] **Elixir Valerianæ Compositum** (*B.P.C.*). *Syn.* ELIXIR BROMIDI ET VALERIANÆ COMPOSITUM.

*Dose*.— $\frac{1}{2}$  to 1 ounce (15 to 30 ml.).

Contains potassium bromide  $7\frac{1}{2}$  gr., chloral hydrate  $7\frac{1}{2}$  gr., and liquid extract of valerian 15 m., with oils of orange, lemon, coriander and anise, in alcohol, syrup and water to 1 oz.

**Extractum Valerianæ** (*B.P.C.*).

*Dose*.—1 to 5 grains (0.06 to 0.3 g.).

The evaporated 70% alcohol percolate.

**Extractum Valerianæ Liquidum** (*B.P.C.*).

*Dose*.—5 to 15 minims (0.3 to 1 ml.). 1 in 1, from freshly dried valerian.

**Infusum Valerianæ Concentratum** (*B.P.C.*).

*Dose*.— $\frac{1}{2}$  to 1 drachm (2 to 4 ml.). 1 in 5

**Infusum Valerianæ Recens** (*B.P.C.*).

*Dose*.— $\frac{1}{2}$  to 1 ounce (15 to 30 ml.). 1 in 40.

Mist. Pot. Brom. et Valerian. (*N.J.F.*). Potassium bromide 10 gr., ammonium carbonate  $2\frac{1}{2}$  gr., concentrated infusion of valerian 30 m., water to  $\frac{1}{2}$  oz.

**Mistura Valerianæ Composita (B.P.C.).**

*Dose.*— $\frac{1}{4}$  to 1 ounce (15 to 30 ml.).

Potassium bromide 10 gr., ammoniated tincture of valerian 10 m., camphor water to 1 oz.

**Mistura Valerianæ Composita (R.F.H.).** Tincture of valerian 3, fetid spirit of ammonia 2, camphor water to 48.

**Tinctura Valerianæ (U.S.P. XI)**

*Average dose.*—60 minims (4 ml.). 1 in 5.

**Tinctura Valerianæ Simplex (B.P.C.)** *Syn.* TINCTURA VALERIANÆ.

*Dose.*—1 to 2 drachms (4 to 8 ml.). 1 in 8.

**Tinctura Valerianæ Ammoniata (B.P.)**

*Dose.*— $\frac{1}{2}$  to 1 drachm (2 to 4 ml.). Valerian 1 in 5, with dilute solution of ammonia 1 in 10, oils of lemon and nutmeg and alcohol 60%. An antispasmodic and nervine tonic.

**Valeriana Indica (B.P.C.),** the dried rhizome and roots of *V. Wallichii*, is used in India and the East in place of valerian, similar preparations being made.

[P1] **Elixir Bromo-Valerianate Gabail (Anglo-French Drug Co, London)** Stated to contain extract of valerian (deodorised) 4.00 g., valerianic acid (deodorised) 1 g., ammonium carbonate 2.5 g., chloral hydrate 4 g., strontium bromide 4 g., syr. aurant. (*Fr. Cx.*) 100 g., distilled water 100 g.

[P1] **Elixir Valibrom (British Drug Houses, London)** Odourless extract of valerian with chloralamide and potassium bromide

[P1] **Elixir Valibrom Compound** contains opium alkaloids equivalent to 0.03% of anhydrous morphine.

**Euvalerol (Allen & Hanburys, London).** Compound elixirs of valerian "A": 1 oz. = 1 dr. of ammoniated tincture of valerian [P1 §1 §4] "B": Elixir "A" with phenobarbitone  $\frac{1}{2}$  gr. per dr. "C": Elixir "A" with ammonium bromide 30 gr. and strontium bromide 15 gr. per oz. *Dose*—1 to 2 teaspoonfuls thrice daily in each case.

**Valerianate (Gabail) (Anglo-French Drug Co, London).** Non-alcoholic extract of valerian root, deodorised. *Dose*—1 teaspoonful 3 or 4 times daily

**Acidum Valerianicum (Fr. Cv, P. Helv. V).**

*Dose.*—1 to 5 minims (0.06 to 0.3 ml.), in syrup or in gelatin capsules

Consists principally of optically inactive isovalerianic acid,  $(CH_3)_2CH \cdot CH_2 \cdot COOH$ , with more or less dextrorotatory methyl-ethylacetic acid,  $(C_2H_5)(CH_3)CH \cdot COOH = 102.1$ .

An oily liquid, sp. gr. about 0.93. Given in hysteria and nervous affections.

**Ammonii Valerianas (Fr. Cx.).** *Syn.* AMMONII VALERAS.

*Dose*—1 to 8 grains (0.06 to 0.5 g.). In masses of flat, colourless, deliquescent crystals, with a strong valerian odour, very soluble in water and alcohol. As supplied commercially it is an acid salt containing ammonia equivalent to only 35% of  $C_4H_9 \cdot COONH_4$ . A 25% aqueous solution is prepared for dispensing.

**Soluté de Valérianate d' Ammoniaque Composé (Fr. Cx.).**

*Dose*—2 to 4 drachms (7 to 15 ml.).

Valerianic acid 3, ammonium carbonate *qs* (about 4) to neutralise, extract of valerian 2, water to 100, all by weight. A "nerve tonic."

**Amyl Valerianate.**  $C_4H_9, C_5H_{11}, C_6H_{13}O_2 = 172.2$ .

*Dose.*—2 to 5 minims (0.12 to 0.3 ml.) in capsules or diluted in alcohol.

The isoamyl ester of isovalerianic acid. A mobile liquid, sp. gr. 0.858. Miscible

with alcohol. Is employed as a sedative and antispasmodic. Has been recommended as gall-stone solvent. Is known as "Apple Essence."

**Ferri Valerianas.**  $\text{Fe}_2(\text{C}_4\text{H}_5\text{O}_2)_2(\text{OH})_2 = 381.9$ . *Syn.* FERRI VALERAS.

*Dose.*—1 to 5 grains (0.06 to 0.3 g.).

A dark red or brown amorphous powder with slight odour. Insoluble in water, soluble in alcohol 90%. A nervine stimulant and emmenagogue, and is used in anæmia.

**Sodii Valerianas** (*B.P.C.*).  $\text{C}_4\text{H}_5\text{O}_2\text{Na} = 124.1$ . *Syn.* SODII VALERAS.

*Dose.*—1 to 5 grains (0.06 to 0.3 g.).

In white hygroscopic masses, soapy to the touch. Used as a nervine sedative

**Zinci Valerianas** (*B.P.C.*).  $(\text{C}_4\text{H}_5\text{COO})_2\text{Zn} \cdot 2\text{H}_2\text{O} = 303.6$ . *Syn.* ZINCI VALERAS.

White powder or in pearly crystals with valerianic odour and sweet astringent taste.

**Soluble** 1 in 120 of water, 1 in 60 of alcohol 90%, 1 in 500 of ether.

**Incompatible.** Acids and metallic salts. (*See also* zinc salts.)

This is given as a nerve and general tonic, *e.g.*, after hay-fever, and as prophylactic, but pharmacologists say it has no efficacy.

**Bornyl Valerianate.** *Syn.* BORNEOL 150-VALERIANATE

*Dose.*—4 to 12 grains (0.25 to 0.75 g.). May be given in 4-gr. capsules

A valerian substitute given in neurasthenia, hysteria, etc. Borneol diminishes reflex irritability, while the valerianic acid is antispasmodic.

**Neo-Bornyl** (*Riedel-de Haen, Berlin; Old Strand Chemical Co., London*). Valerylglucolic ester of borneol. Perles contain 0.25 g. *Dose.*—1 or 2 perles twice or thrice daily. Cardiac neurosis, nervous gastric troubles, etc.

**[D-P-1-81] Trivalin** (*Saccharin Corporation, London*). *Dose.*—Hypodermically, 8 to 15 minims ( $\frac{1}{2}$  to 1 ml.) once to 3 times daily. A solution containing per ml. 0.0037 g. ( $\frac{1}{2}$  gr.) of caffeine valerianate, 0.0054 g. ( $\frac{1}{2}$  gr.) of cocaine valerianate and 0.0019 g. ( $\frac{1}{4}$  gr.) of morphine valerianate. Also available in capsules. Said to have the therapeutic effects of morphine without disadvantages. Anodyne, *e.g.*, in painful dressings, inoperable cancer, gallstone colic and neuralgia. As a tonic in delirium, mania and hysteria.

The combination is in the proportion of one molecule each of caffeine valerianate and cocaine valerianate and 4 molecules of morphine valerianate

Is also made in combination with hyoscine valerianate  $\frac{1}{10}$  grain (0.00056 g.) per ml., for treatment of the insane. *Dose.*—0.25 to 0.5 ml. daily.

**Valisan** (*Schering, London*). Borneol ester of bromosovalerianic acid *Dose.*—2 or 3 perles of 3.75 grains several times a day.

**Valyl** (*Bayer Products, London*) Valeryldiethylamide *Dose.*—2 or 3 perles of 0.125 g. several times a day.

**Castor** (*B.P.C., P. Austr.*).

The dried preputial follicles and secretions from the beaver, *Castor fiber* (*Rodentia*), in brown pieces. *Fr. Cx.* describes the two commercial varieties, Canadian and Russian. Contains from 35 to 70% of alcohol-soluble matter. Stimulant and antispasmodic. Is given in dysmenorrhœa as tincture.

**Tinctura Castorei** (*B.P.C.*).

*Dose.*— $\frac{1}{2}$  to 1 drachm (2 to 4 ml.). 1 in 20. It must be suspended in water with mucilage of acacia.

**Gutta Castorei Compositæ.** Tincture of castor 1 oz., compound tincture of chloroform 4 dr., compound tincture of lavender 1 oz., spirit of camphor 4 dr., spirit of nitrous ether 1 oz. A teaspoonful in water for nervousness or sleeplessness.

**Sumbul** (*B.P.C.*). *Syn.* MUSK ROOT. Dried transversely sliced root of *Ferula Sumbul* (*Umbelliferae*). Used as nervine sedative and anti-hysterical.

**Tinctura Sumbul (B.P.C.).**

*Dose.*— $\frac{1}{4}$  to 1 drachm (2 to 4 ml.). 1 in 10. When diluted it requires addition of mucilage of acacia to suspend the resin.

**ZINCUM**

Zn = 65.38.

To prepare arsenic-free, melt in a clay crucible and add, in small bits at intervals, about 15 grains of sodium to a pound. Remove the scum, avoiding iron implements, and repeat in another clean crucible. Granulate by pouring into water.

**Incompatibilities of Zinc Salts.** Alkaline carbonates, and alkalis in general, vegetable infusions and milk.

**Antidotes.** Do not use emetic or stomach tube, patient is probably vomiting. Give copious draughts of sodium or potassium bicarbonate dissolved in warm water. Keep patient lying down; apply heat to abdomen. Give demulcents, such as milk and eggs, freely. Tannic acid or medicinal charcoal has been used. Morphine,  $\frac{1}{4}$  gr. hypodermically, if pain is severe.

Abnormal amounts of zinc may enter and leave the body for years without causing symptoms detectable clinically or by laboratory examinations.—*Lancet*, 11/1926, 530.

**Zinci Acetas (B.P.C., U.S.P. XI).**

$\text{Zn}(\text{CH}_3\text{COO})_2 \cdot 2\text{H}_2\text{O} = 219.5$ .

*Dose.*—1 to 2 grains (0.06 to 0.12 g.) as a nervine tonic, but pharmacologists have no evidence of its utility. 10 grains (0.6 g.), or more, as an emetic.

White crystals with faint acetous odour. Soluble 1 in 2.5 of water, about 1 in 40 of alcohol 90%. Used as astringent lotion ( $\frac{1}{4}$  to 1%).

**Zinci Bromidum (B.P.C.).**  $\text{ZnBr}_2 = 225.2$ .

*Dose.*—2 to 5 grains (0.12 to 0.3 g.) in water.

White deliquescent powder. Soluble 4 in 1 of water, 2 in 1 of alcohol 90% and in ether. A little dilute hydrobromic acid will make a clear solution. Incompatible with alkaloids, salts of heavy metals, borax and alkali carbonates. Has been used with success in epilepsy.

**Zinci Carbonas (B.P.C.).** *Syn.* ZINC SUBCARBONATE. A white impalpable powder varying slightly in composition but approximately corresponding to  $\text{ZnCO}_3 \cdot 2\text{ZnO} \cdot 3\text{H}_2\text{O}$ . Insoluble in water and alcohol. Mildly astringent and protective, and occasionally used similarly to the oxide in lotions or dusting powders.

**Zinci Chloridum (B.P., U.S.P. XI, P. *Helv.* V, P: *Dan.*).**

$\text{ZnCl}_2 = 136.3$ .

In deliquescent sticks, masses or granular powder. Owing to presence of oxychloride it is not completely soluble in water, but solutions clear on neutralising to methyl orange with hydrochloric acid.



**Soluble** 1 in less than 1 of water, 1 in about  $1\frac{1}{2}$  of alcohol 90%, 1 in 2 of glycerin.

**Uses.** A powerful, odourless caustic, astringent, antiseptic and anti-putrescent. As a lotion for wounds and ulcers 10 to 20 gr. per oz. is used. A paste prepared with starch and glycerin is sometimes used in lupus and for ulcers. As an astringent antiseptic in ophthalmology, solutions containing  $\frac{1}{2}$  to 2 gr. per oz are used.

In the treatment of erosion of teeth, is useful to touch painful spots, or the addition of a little to chloroform-mastic forms a useful paint.—Smale and Colyer. (The zinc chloride must be dissolved in a small quantity of dehydrated alcohol, with a trace of hydrochloric acid if necessary, and added to the chloroform-mastic solution.)

**TUBERCULOUS ULCERATION.** Pain abolished and ulcerations healed after 5 applications of solution of 3 g zinc chloride in 10 ml of 80% alcohol Repeat every 3 weeks: tincture of iodine applied daily —Per *J Amer med Ass*, 1/1927, 1039.

**Collutorium Astringens (R.D.H.).**

Zinc chloride 5 gr., zinc sulphate 10 gr., water to 1 oz.

**U.C.H.** uses zinc chloride 0.4, zinc sulphate 0.4, spirit of chloroform 0.4, aniline yellow q.s., dilute hydrochloric acid 0.15, peppermint water to 100 Use half a teaspoonful to half a tumblerful of water.

**Collyrium Zinci Chloridi (B.P.C.).** 0.1% w/v

**Guttæ Zinci Chloridi (R.L.O.H., St T H.).**  $\frac{1}{2}$ , 1 or 2 gr. per oz

**Guttæ Zinci Chloridi cum Alcohol (Brompton H.)** Zinc chloride 5 gr., alcohol 90%  $\frac{1}{2}$  oz., water  $\frac{1}{2}$  oz. For Eustachian self-inflator

[D.P1-81] **Guttæ Zinci Chloridi cum Cocainæ Hydrochlorido.**

$\frac{1}{2}$ , 1 or 2 gr with cocaine hydrochloride 10 gr per oz

**Injectio Zinci Chloridi (L.H.).** For vaginal use

Zinc chloride 5 gr., water to a pint.

**Liquor Zinci Chloridi (B.P.C.).**

Contains the equivalent of about 40% w/v of zinc. Sp. gr. 1.53. 4 m of this solution = 3 gr. of solid zinc chloride On diluting, a trace of hydrochloric acid will be necessary to clear it.

**Lotio Zinci Chloridi (R.L.O.H.).**  $\frac{1}{2}$  or 1 grain to 1 ounce.

**Zinci Oxidum (B.P., U.S.P. XI, P. Helv. V, P. Dan.).**  
ZnO = 81.38.

**Dose.**—5 to 10 grains (0.3 to 0.6 g.). Tablets, 2 grains.

Has been used for nervous debility, migraine, hysteria, and for the night-sweats of phthisis. Chiefly employed externally as a mild astringent and protective in ointments, lotions and dusting powders for skin affections.

**Soluble** in sodium hydroxide solution and in mineral acids; insoluble in water and alcohol 90%.

Has definite bactericidal properties. While it is almost neutral so far as the cells of the skin are concerned, it is split up by acid-producing microbes into disinfectant compounds.—Haxthausen, per *Prescriber*, 1929, 330.

**Cremor Zinci (B.P.C.).** Zinc oxide 32% in wool fat, almond oil and solution of calcium hydroxide.

**Cremor Zinci (St. M. H.).**

Zinc oxide 480 gr., wool fat 3 dr, olive oil 1 oz, solution of calcium hydroxide 1 oz. Useful in acute eczema in the drying stage where there is much redness

**Cremor Zinci cum Calamina (Mid. H.).** Zinc oxide 30 gr., calamine 30 gr., thymol 2 gr., hydrous wool fat 2 dr., liquid paraffin to 1 oz. For eczema of the meatus

**Emplastrum Zinci Oxidi (B.P.C.).** Spread with a rubber adhesive compound containing not less than 20% of zinc oxide

**Gelatinum Zinci (B.P.).** *Syn.* UNNA'S PASTE.

Zinc oxide 15% in a glycerin-water-gelatin base. For use it is melted and applied with a brush to eczematous surfaces. Ichthammol, resorcinol and other medicaments may be added.

VARICOSE ULCERS treated by the above after thoroughly cleansing the leg or foot with soap and spirit, alcohol, mercuric chloride solution 1 in 2000 to 1 in 4000, or 1 in 40 carbolic lotion. The paste, previously melted and cooled, is poured over the ulcer. The part is then dried and the paste is bandaged on with a gauze bandage. Another layer of paste is applied, this is covered with a bandage, and so on until four layers have been applied. May be left in many cases undisturbed for weeks, but it is safer to dress again after 2 or 3 days with salicylic talc if any discharge. It forms a new skin, pliable and slightly elastic.

A preparation of the composition zinc oxide 1, gelatin 2, glycerin 3, water 4 parts, of value in arthritis, dermatitis, erysipelas, erythema nodosum and simplex, myositis, periostitis, phlebitis and varix of the leg, synovitis, "tennis leg," minor thrombosis, and contusions and sprains of joints or limbs. It is the treatment *par excellence* for chronic varix and acute phlebitis. Method of preparation and application of dressings—W Muir Smith, *Brit med. J.*, 1/1927, 137.

[P2] **Gelatin Compound Phenolised.** Gelatin 625 parts, zinc oxide 250, glycerin 1900, water 1900 containing 1.5% of phenol. Heat till liquid and apply with brush, apply spiral bandage, and brush on another layer, repeat to total of three bandages and four layers of the preparation. For chronic ulcers, unhealed secondary burns and varicose veins—*J Amer med Ass.*, 11/1929, 1809.

A further modified form. Zinc oxide 10, glycerin 10, glue 4, acacia 5, water 30. Spread on bandages for varicose ulcers—C. J. and K. M. Cellan-Jones, *Brit med. J.*, 11/1930, 560.

Varicose ulceration well treated by moist paste bandage of Cellan-Jones—E. Garden, *Brit med. J.*, 1/1931, 652.

**Gelatinum Zinci et Ichthammolis (B.P.C.).** *Syn.* PASTA ZINCI ET ICHTHAMMOLIS. Ichthammol 2% in a zinc oxide and glyco-gelatin basis.

**Ligamentum Pastæ Zinci (B.P.C.).** *Syn.* ZINC PASTE BANDAGE. Prepared with a paste containing not less than 17% of zinc oxide.

**Lot. Calamin Co. (N I F)** Calamine 3 dr, zinc oxide 3 dr, glycerin 3 dr, solution of calcium hydroxide to 8 oz.

**Pasta Carbonis et Zinci.** Soak gelatin 16 in a portion of the total glycerin required (20), and a portion of the water (50 in all required), for 12 hours. Make a paste of boric acid 6, zinc oxide 6 and charcoal 18 with remainder of liquids, mix on water-bath, and pour into suitable vessel to set.

For leg ulcers the charcoal is a useful addition. Boric lotion fomentation should first be carried out to clean the ulcer. If tending to be sluggish red lotion helps.

**Pasta Zinci cum Amylo (St. M. H)**

Zinc oxide, starch, liquid paraffin, wool fat, of each equal parts. For inter-trigo and disordered perspiration.

**Pasta Zinci Oxidi Composita (B.P.).** *Syn.* ZINC PASTE.

Zinc oxide and starch, of each 25%, in white soft paraffin.

**Pasta Zinci Oxidi cum Acido Salicylico (B.P.C.).** *Syn.* LASSAR'S PASTE.

Salicylic acid 2% in a zinc oxide, starch, and white soft paraffin paste.

Useful in chronic and acute eczema when weeping. In irritating conditions the acid may be omitted. It may be retained and increased in amount where there is less inflammatory reaction and where much scaling has occurred.

**Petrolatum Zinci Oxidi.** Zinc oxide 1, white soft paraffin 9 For surgical use starch is sometimes added, *cf.*, *Pasta Zinci cum Amylo.*

[P1] **Pilulæ Zinci Oxidi et Belladonnæ (B.P.C.)**

*Dose.*—1 pill.

Contains zinc oxide 2 gr. and extract of belladonna  $\frac{1}{4}$  gr.

[P1] **Pilula Zinci cum Belladonna (T.H.).**

Zinc oxide 2 gr., extract of belladonna  $\frac{1}{2}$  gr. *Dose*—1 or 2 at bedtime

**Pulvis Zinci et Acidi Borici (B.P.C.)**

Equal parts of zinc oxide and boric acid.

**Pulvis Zinci et Amyli (B.P.C.).**

Equal parts of zinc oxide and starch.

**Pulvis Zinci et Amyli Compositus (B.P.C.).**

Equal parts of zinc oxide, starch, boric acid and purified talc, perfumed with oil of geranium

**Unguentum Benzoini et Zinci (C.X.H.).** Compound tincture of benzoin 2, ointment of boric acid 4, ointment of zinc oxide 4, olive oil 1 Gives relief in, and stimulates healing of, cracked nipples and small ulcers and fissures

**Unguentum Wilsoni (P. Jap. IV). Syn WILSON'S OINTMENT**

Zinc oxide 5, benzoic acid 1, lard 30.

**Ung. Z.E.B. (N.I.F.).** Ointment of zinc oxide 146 gr., oil of eucalyptus 18 m., yellow ointment of boric acid (N.I.F.) to 1 oz.

**Unguentum Zinci Carbolisatum.** Zinc oxide 10, phenol 2, soft paraffin 88. Dermatitis is well treated with this.

**Unguentum Zinci cum Acido Salicylico.**

Salicylic acid 40 gr., zinc ointment 1 oz., soft paraffin 1 oz.

**Unguentum Zinci cum Balsamo Peruviano (B.P.C.).**

Balsam of Peru 4% in ointments of zinc oxide and boric acid.

**Unguentum Zinci cum Benzoino (B.P.C.).**

Compound tincture of benzoin about 1 in 8 in ointment of zinc oxide.

**Unguentum Zinci et Olei Ricini (B.P.C.).**

Zinc oxide and castor oil in benzoinated lard, corresponding to a mixture of equal weights of castor oil and the zinc ointment of the *B.P.* '14.

**Unguentum Zinci et Olei Ricini cum Benzoino (B.P.C.).**

Zinc oxide, castor oil and compound tincture of benzoin in benzoinated lard.

**Unguentum Zinci Oxidi (B.P.).** *Syn.* UNGUENTUM ZINCI. Zinc oxide 15% in simple ointment. Does not mix with castor oil (*see* Unguentum Zinci et Olei Ricini).

The zinc ointment of the *B.P.* is, on the whole, the most generally suitable for all forms of dermatitis—H. Haldin-Davis, *Brit. med. J.*, 1/1935, 289.

**Unguentum Zinci Oxidi (U.S.P. XI).**

Zinc oxide 20, liquid petrolatum 10, wool fat 5, white wax 5, white petrolatum 60.

**Unguentum Zinci Oxidi Compositum** (*St. T. H.*) *Syn.* IGNOFORM OINTMENT.

Zinc oxide 100 gr., cocoa butter 10 gr., solution of hamamelis 10 m., distilled water 80 m., wool fat 150 gr., yellow soft paraffin to 1 oz.

**Pellanthum** (*Handford & Dawson, Harrogate*). A water-soluble artificial skin containing 20% of zinc oxide. For skin affections. Is also available with ichthammol and in other combinations.

[P1] **Proctoids** (*Petrolagar Laboratories, London*). Suppositories containing zinc oxide 10, boric acid 10, bismuth oxyiodide 1.67, bismuth carbonate 8.33, powdered extract of belladonna 0.5, ephedrine sulphate 0.1, balsam of Peru 1.0, cocoa butter to 100. For hæmorrhoids, pruritus ani, fistula, etc.

**Zinc Oxychloride.** Used as a dental filling. The "powder" is of zinc oxide and the "liquid" zinc chloride solution. Mix thoroughly. Sometimes used as a root-filling and for sensitive dentine; will irritate a live pulp. The following are also used —

**Zinc Oxyphosphate.** It is supplied in the form of dried powdered zinc oxide in various colours, with the "liquid," which consists of phosphoric acid. These are mixed intimately prior to use as a flooring when not too near the pulp.

**Zinc Oxysulphate.** Consists of calcined zinc sulphate and zinc oxide; mucilage of acacia is used to mass.

Fletcher's Artificial Dentine is similar

**Zinci Sulphas** (*B.P., U.S.P. XI, P. Helv. V, P. Dan.*).

$\text{ZnSO}_4 \cdot 7\text{H}_2\text{O} = 287.55$ .

Dose.—1 to 3 grains (0.06 to 0.2 g.); emetic dose 10 to 30 gr (0.6 to 2 g.) *Fr. Cx.* has max. single and daily dose 15 grains.

**Soluble** 1 in 0.65 of cold water, 5 in 1 of boiling water; insoluble in alcohol 90%

**Uses.**  $\frac{1}{2}$  to 1% solutions, frequently combined with alum or sometimes ferrous sulphate, are used for inflammatory conditions of the mucous membrane, e.g., gleet and gonorrhœa. 1 in 500 may be added to eye lotions in conjunctivitis

Smarting of zinc or copper salts in collyria may be relieved by using a saturated solution of potassium chlorate instead of water.—*Brit. med. J.*, 1/1926, 928.

**Zinc Sulphate Points** are moulded for intra-uterine use. Points of equal parts zinc sulphate and alum, and of copper sulphate are also made.

**Collyrium Astringens Luteum** (*P. Austr.*, 1906). *Syn.* GUTTÆ HORSTI, HORST'S EYE WASH.

Ammonium chloride 2, zinc sulphate 5, distilled water 890, dissolve and add camphor 2, dissolved in diluted spirit (sp. gr. 0.895) 100, then add saffron 1. Digest 24 hours and filter. As an astringent lotion it is used for conjunctivitis.

**Collyr. Zinci Co.** (*N.I.F.*). Boric acid 5 gr. and zinc sulphate 1 gr. per oz.

**Collyrium Zinci Sulphatis** (*B.P.C.*). 0.2% w/v.

**Guttæ Zinci Sulphatis** (*R.L.O.H.*).  $\frac{1}{2}$ , 1 or 2 gr. per oz

**Injectio Zinci Sulphatis** (*L.H.*). For vaginal use.

Has 60 grains in 1 pint of water, i.e., 0.69% or 1 in 144.9

**Lotio Potassæ Sulphuratæ** (*B.P.C.*) *Syn.* LOTIO ZINCI SULPHIDI, LOTIO ALBA.

Contains zinc sulphide freshly precipitated by interaction of 10 gr. of sulphurated potash and 10 gr. of zinc sulphate per oz. of rose water. Acne vulgaris is well treated with this.

**Lotio Rubra** (*B.P.C.*). Contains zinc sulphate 2 gr., with compound tincture of lavender and water to 1 oz. *R.L.O.H.* is similar but with 1 gr. of zinc sulphate per oz.

[P2] **Lotio Spiritus Sulph. Co. (L.S.H.).** Zinc sulphate 30 gr., sulphurated potash 30 gr., water to 3 oz.; mix and add phenol 1 dr., resorcinol 1 dr., industrial methylated spirit to 6 oz.

**Lotio Sulphatam.** Zinc sulphate 30 to 40 gr., alum 30 to 40 gr., ferrous sulphate 20 gr., copper sulphate 2 gr., water to 8 oz.

**Lotio Sulphuris cum Zinco (St. J. H.).** Precipitated sulphur 15 gr., zinc sulphate 15 gr., sulphurated potash 15 gr., water to 1 oz.

**Lotio Zinci Sulphatis.** Zinc sulphate 0.25 or 0.5% in distilled water

**Pessus Zinci Sulphatis (B.P.C.)** contains 5 gr. (0.3 g.).

**Pulvis Zinci Sulphatis Compositus (B.P.C.).** *Syn.* PULVIS ACIDI BORICI COMPOSITUS, PULVIS ANTISEPTICUS SOLUBILIS

Zinc sulphate, 1 in 8, with eucalyptol, menthol, phenol, thymol, salicylic acid and boric acid.

**Calamina (B.P.C.).** *Syn.* CALAMINA PRÆPARATA.

A basic zinc carbonate, with or without zinc oxide, yielding 68 to 90% of residue (ZnO) on ignition, and suitably coloured with iron oxide. It was formerly obtained by igniting the native carbonate, but is now prepared by precipitation.

**Linimentum Calaminæ (B.P.C.).**

Calamine about 20 gr. and zinc oxide about 15 gr. in an emulsion of liquid paraffin and solution of calcium hydroxide to 1 oz. This preparation has the advantage over similar preparations made with vegetable oils of not becoming thicker on storage.

In chronic eczema, e.g., to a freely-weeping surface with redness and itching, apply with brush or cotton-wool swab, or spread on thin washed butter muslin. Very important that the inflamed surface should not be treated with a hot thick dressing. Perchloride 1 in 2000 to 1 in 3000 may be a desirable addition.

**Linimentum Calaminæ (L.S.H.)** Calamine 40 gr., zinc oxide 20 gr., solution of calcium hydroxide and sesame oil of each  $\frac{1}{2}$  oz.

*St. G. H.*—Calamine 30 gr., zinc oxide 30 gr., glycerin of lead subacetate 6 m., olive oil  $\frac{1}{2}$  oz., solution of calcium hydroxide to 1 oz.

*W. H.*—Calamine 30 gr., zinc oxide 30 gr., wool fat 4 gr., oleic acid 3 m., liquid paraffin  $\frac{1}{2}$  oz., solution of calcium hydroxide to 1 oz.

*P. E. H. C., St. M. H.* (Lotio Calaminæ Oleosa)—Calamine 40 gr., zinc oxide 20 gr., solution of calcium hydroxide 3 dr., olive oil to 1 oz.

*St. T. H.*—Calamine 40 gr., zinc oxide 30 gr., oil of lavender 1 m., solution of calcium hydroxide  $\frac{1}{2}$  oz., arachis oil 225 m.

**Linimentum Calaminæ Compositum (B.P.C.)**

Calamine 43 $\frac{1}{2}$  gr., zinc oxide about 22 gr. and zinc oleostearate about 11 gr. in wool fat, white soft paraffin and liquid paraffin to 1 oz.

**Linimentum Calaminæ Compositum (U.C.H.).** Prepared calamine 9, zinc oxide 5, zinc oleostearate 3, wool fat 3, soft paraffin 20, liquid paraffin to 100

**Lotio Calaminæ (B.P.C.).**

Calamine about 65 gr. and zinc oxide about 22 gr. with glycerin and rose water to 1 oz.

The desirability of closer co-operation between those responsible for the compilation of hospital pharmacopœias is suggested by the numerous small differences in the following formulæ for this lotion.

*C.X.H.*—Calamine 15 gr., zinc oxide 10 gr., glycerin 30 m., solution of calcium hydroxide 80 m., water to 1 oz.

*Gt. Orm. H.*—Zinc oxide 30 gr., calamine 30 gr., glycerin 24 m., solution of calcium hydroxide 24 m., water to 1 oz.

*L.S.H.*—Calamine 20 gr., zinc oxide 20 gr., glycerin 30 m., solution of calcium hydroxide 5 dr., water to 1 oz.

*Mid. H.*—Calamine 30 gr., zinc oxide 20 gr., glycerin 15 m., water to 1 oz.

*P.E.H.C.*—Calamine 40 gr., zinc oxide 20 gr., glycerin 20 m., water to 1 oz.

*St. G. H.*—Calamine 30 gr., zinc oxide 30 gr., glycerin of lead subacetate 5 m., glycerin 30 m., water to 1 oz.

*St. J. H.*—Calamine 20 gr., zinc oxide 20 gr., glycerin 30 m., solution of calcium hydroxide  $\frac{1}{2}$  oz., water to 1 oz.

*St. M. H.*—Calamine 30 gr., zinc oxide 30 gr., glycerin 30 m., solution of calcium hydroxide to 1 oz.

*St. T. H.*—Calamine 20 gr., zinc oxide 20 gr., glycerin 24 m., solution of calcium hydroxide 1 dr., water to 1 oz.

*U.C.H.*—Calamine 9, zinc oxide 5, glycerin 3, water to 100.

*W.H.*—Calamine 60 gr., glycerin 10 m., solution of calcium hydroxide 2 dr., water to 1 oz.

Used in eczema, especially where the surface is red and tender, also to conceal acne spots on the face [P2] Mercuric chloride 1 gr may be added to 6 oz. as antiseptic

For chilblains, sunburn, etc., this lotion or the liniment made double or treble strength, allays the intense irritation

### Unguentum Calaminæ (B.P.C.)

Calamine 1 in 6 in yellow soft paraffin.

[P1 81] **Unguentum Plumbi cum Calamina** (*St. G. H.*). *Syn* ERYSIPELAS DRESSING.

Plaster of lead 3 dr., calamine 20 gr., olive oil 90 m., lard to 480 gr

**Stannum.** Sn = 118.7 Given internally, pure tin powder is probably not absorbed. Was formerly used as a tæniacide. From 4 to 15 g. were given suspended in syrups or made into an electuary and followed in from 3 to 6 hours by a brisk cathartic. Some of the salts (chiefly chloride) are credited with vermicidal properties. In dose of  $\frac{1}{16}$  to  $\frac{1}{2}$  grain the chloride has been used as an antispasmodic in chorea, epilepsy and other convulsive diseases.

**Stanni Oxidum** (Stannic Oxide).  $\text{SnO}_2 = 150.7$

*Dose*—8 to 15 grains (0.5 to 1 g.) daily.

A white or greyish-white powder insoluble in water and hydrochloric acid, soluble in alkalis, forming stannates. Administered for staphylococcal infections. Used chiefly technically and diluted as a cosmetic, e.g., as nail polish.

Distinguish from stannous oxide,  $\text{SnO}$ , which is dark grey—nearly black.

“Putty powder” is usually a mixture of tin and lead oxides or a stannate of lead, used for polishing glass.

**Jungman's Tooth Powder.** Tin (stannic) oxide 15, calcium carbonate 60, soap 4, sugar 5. Flavour with 6 drops of a mixture of equal parts of oil of wintergreen and oil of sassafras per 100 g. of powder; mix these first with the sugar. —*Pharm. J.*, 1/1922, 263.

**Tab. Stann. Co.** (*N.I.F.*) “Stann. 1.7 gr., Stanni Oxid. 0.3 gr.”

**Staniform** (*Staniform Ltd., London*). Preparations containing methyl stannic iodide. Available as ointment, dusting powder, lotion and tablets. For treatment of boils, ulcers, carbuncles, whitlows, acne, eczema, burns, chilblains, etc.

**Stannoxyd** (*Robert et Carrière, Paris; Anglo-French Drug Co., London*)

Preparations of metallic tin, tin oxide or tin salts for the treatment of boils, carbuncles, acne, styes and all staphylococcal infections. Harmless and prompt in action, definite results being obtained in 5 to 6 days. **Tablets** contain metallic tin 42½% and tin oxide 7½%. *Dose*—4 to 8 daily. May be supplemented by local applications of the following—**Liquid** contains 25% of tin protochloride. Used as a 2 to 4% solution in water. **Glycerin** contains 2% of the chloride in glycerin. For use in furunculosis of the nasal and aural passages. **Ampoules**, containing equivalent of 0.004 g. of metallic tin in 2 ml., for hypodermic or intramuscular injection. A **Bath** and **Gauze** are also prepared.

Small quantities of tin act as catalyst and assist synthesis of fatty acids and glycerin into fat. 2 ml. of Stannoxyd intramuscularly, in conjunction with 1 drachm of glycerin in 1 drachm of boiled water intravenously, gave good results in scirrhus of the breast.—J. T. Shirlaw, *Brit. med. J.*, 1/1931, 74.

**Tin-Ox** (*John Bell, Hulls & Lucas, London*). Combination of tin and tin oxide in tablet form.

**Titan Oxidum**.  $\text{TiO}_2$ . *Syn.* TITANIC OXIDE, TITANIUM DIOXIDE. A white powder insoluble in water, soluble in alkalis and in acids. Used in face powders and other toilet articles in place of zinc oxide.

## ZINGIBER

*B.P., U.S.P. XI, P. Helv. V, P. Dan*

*Dose*.—5 to 15 grains (0.3 to 1 g.).

The dried rhizome (scraped) of *Z. officinale* (Scitamineæ).

Must yield not less than 4.5% to alcohol 90%, and not less than 10% to water; *U.S.P. XI* requires minimum of 4.5% to ether. *P.G. VI* has the rhizome not scraped.

Ginger cultivation in Jamaica.—*Pharm. J.*, 1/1926, 324.

Research by the Imperial Institute has resulted in a high-grade ginger available from Nigeria, equal in all respects to best Jamaica.—*Imp. Inst. Rept.*, 1930.

**Fluidextractum Zingiberis** (*U.S.P. XI*). *Average dose*—10 minims (0.6 ml.). 1 ml. represents 1 g. of ginger, and it contains from 69 to 76% v/v of alcohol.

**Oleoresina Zingiberis** (*B.P.C.*) *Syn.* GINGERIN

*Dose*.—¼ to 1 grain (0.015 to 0.06 g.).

The acetone-soluble matter of ginger.

**Syrupus Zingiberis** (*B.P.*).

*Dose*.—½ to 2 drachms (2 to 8 ml.).

Strong tincture of ginger 1, syrup q.s. to produce 20.

**Tinctura Zingiberis Fortis** (*B.P.*). *Syn.* ESSENCE OF GINGER.

*Dose*.—5 to 10 minims (0.3 to 0.6 ml.).

1 in 2 by percolation with alcohol 90%.

**Tinctura Zingiberis Mitis** (*B.P.*). *Syn.* TINCTURA ZINGIBERIS.

*Dose*.—½ to 1 drachm (2 to 4 ml.).

Strong tincture of ginger, 1 in 5, with alcohol 90%

**Curcuma** (*B.P.C.*). *Syn.* TURMERIC ROOT.

The dried rhizome of *C. domestica* (Zingiberaceæ). Used in curry powders and condiments. **Tinctura Curcumæ**, 1 in 6, is used as a colouring agent and for the preparation of turmeric paper.

**Zedoary**, the rhizome of *Curcuma Zedoaria* (Zingiberaceæ), resembles ginger in odour and taste.

## VACCINES, SERA, TOXINS AND ANTITOXINS

**Immunity** to infectious diseases may be (1) *natural* where the host is naturally insusceptible to the infection; (2) *acquired* (a) developed as result of recovery from infectious disease, or by artificial introduction of gradually increased doses of bacteria or toxin—this is *active immunity*, (b) produced by introducing an antibody to the infecting substance in the shape of serum from an animal previously immunised—this is *temporary* or *passive immunity*. When a person is exposed to infectious disease there may be natural immunity, or he may acquire same and develop power to resist the poison. On recovery, immunity will persist for a longer or shorter time, rendering him less liable to contract the disease again.

Immunity reaction consists essentially in the exercise of certain capacities of *defence* on the part of the body cells in response to the exercise of certain capacities of *offence* on the part of the infecting micro-organisms

**Antibody** is a substance found in the blood serum, resulting from the inoculation into the animal of a foreign *protein* termed an *antigen*. Thus, if a foreign protein, e.g., egg albumen, be injected, the blood serum acquires a new property, that of precipitating a solution of egg albumen such as was used for the injection. Here the albumen is the antigen, and the new property is assumed to be due to a new substance—an antibody called *precipitin*. Antibodies are always *specific*, for example, diphtheria toxin acting as an antigen leads to the production of diphtheria antitoxin which has no action on the toxin of tetanus. Antibodies may be classified according to the effects produced on combining with corresponding antigens, thus:—

Antibody.	Antigen.	Action.
Antitoxin	Toxin	Neutralisation.
Precipitin	Coagulable protein	Precipitation.
Agglutinin	Cells, bacteria, etc.	Clumping.
Cytolysin (including Bacteriolysin and Hæmolysin)	Cells, bacteria, etc.	Prepares cells, bacteria, etc., for solution by complement
Opsonin	Cells, bacteria, etc	Prepares cells, bacteria, etc., for ingestion by phagocytes.

It is not certain that opsonin should be classed as an antibody. Possibly all the true antibodies play the part of an opsonin.

Two substances are required for the lysis of the microbe—the so-called *immune body* produced during the injection treatment, and the other, known as the *complement*, which exists already in normal serum and is not elaborated in increased quantities by the injections. The immune body is supposed to possess two affinities, one of which binds it to the bacterium, and the other satisfies itself by combining with the complement. The possession of this double affinity of the bacteriolysin is recognised in its name of amboceptor. It must be regarded as an intermediary body which, on being added to the



bacteria during the process of immunisation, gives the complement, existing already in the blood serum, the power of attacking them. The complement, not the immune body, destroys the bacteria.

The antigens in common use for the production of *artificial active immunity* include bacterial vaccines, toxins, toxoids, anti-viruses and bacteriophages. The antibodies used for temporary passive immunity are usually derived from the serum of horses immunised to the particular infection, and are either antitoxic or antibacterial in effect.

**Vaccine Therapy** may be defined as—"to exploit in the interest of infected tissues the unexercised immunising capacities of the uninfected tissues"—in other words, to stimulate the chemical machinery of the patient to elaborate the required specifically bacteriotropic substances. Vaccines have given valuable results in the prophylaxis of a number of diseases. In the treatment of some infections, *e.g.*, furunculosis and other staphylococcal infections, and in bronchitis and other infections of the respiratory tract due to the pneumococcus, the results have been striking. In many other diseases, such as typhoid fever, and in gonococcal, staphylococcal and streptococcal infections, encouraging observations are on record.

**Antitoxin Treatment** is based on the observation of Behring, who showed that the toxin of the diphtheria bacillus when injected into a suitable animal effected an immunity, that *the serum of this animal gave protection against the disease when injected into another, and that it could be employed for treating the disease in the human body.*

The antitoxins contained in this animal blood serum combine with the toxins in the blood and tissues of the sick person, by so doing they *neutralise the power of the toxins*, and thus he recuperates.

The toxins of diphtheria and tetanus are examples of extra-cellular "soluble" toxins (exotoxins) excreted by the bacteria, and found in the fluids in which they are cultivated. In the case of typhoid and plague, the toxins are apparently inherent in the bacterial cell; these are examples of endotoxins. Anti-endotoxins are not readily produced.

In *antitoxin treatment*, a serum which already contains the antitoxin is introduced into the patient's circulation, and this has the power of uniting with the toxin to form an inert substance (passive immunity). Contrast this with *vaccine treatment*, wherein the tissues of the body are stimulated to form the necessary antibodies for themselves (active immunity)

## VACCINES

The ordinary type of bacterial vaccine is a suspension (emulsion) of the killed or attenuated bacteria in normal saline with, as a rule,  $\frac{1}{2}\%$  of phenol or cresol as antiseptic.

Bacterial vaccines may be either (a) **Autogenous**, that is, prepared from cultures of the organisms obtained from the patient, or (b) **Stock vaccines** prepared from stock cultures. Opinions differ as to the relative merits of the two types. For *prophylaxis* it is obviously not possible to have an autogenous vaccine. For *treatment*, autogenous vaccines should, if possible, be used (a) when the infecting agent belongs to an ill-defined group, e.g., *B. coli* infections; (b) when the infection is severe and it is felt to be too great a risk to wait and see whether stock vaccine is effective; (c) when treatment with stock vaccine has failed.

In the case of *B. tuberculosis* an autogenous vaccine is not essential, and there are many obstacles in the way in other diseases, e.g., in gonorrhœa it may be difficult to secure a pure culture, and the loss of time may be of immense importance. In some cases a stock vaccine is used while a special one is being prepared from the case.

### Technique of Injecting a Vaccine.

The skin should be sterilised with iodine or diluted lysol or other disinfectant; too strong applications should be avoided. The best sites are: (1) the arm, preferably the upper arm near the insertion of the deltoid, (2)  $1\frac{1}{2}$  inches below the centre of the clavicle; (3) high up on the buttock near the spine; (4) the flank.

The inoculation may be made into the subcutaneous tissue. The ampoule should be shaken before use, as the emulsions settle.

### Local and General Effects of the Injection.

#### (a) Local —

In 12 to 24 hours there may be some redness, swelling, pain, and tenderness at the site of inoculation, and for an area of 2 to 3 inches around it.

#### (b) General Effects —

(1) One of the results is the production of a local hyperæmia round and in the infected focus, this is best seen in cases of iritis, laryngitis and acute skin infections. (2) Other effects are a rise in temperature in about 12 hours, which should not exceed  $1\frac{5}{8}^{\circ}\text{F.}$ , a rise in pulse rate, which should not exceed 20 beats, a slight feeling of malaise and perhaps a little headache, these should all pass off within 24 hours if the temperature and pulse were previously unduly high, they should then assume a better level, and the malaise and headache should be succeeded by a feeling of increased well-being.

Other clinical symptoms should also improve. If none of these result, the dose employed was too small.

The signal for reinoculation is retrogression of the patient or failure to continue to improve.

Increase of dosage is indicated by failure to secure any general reaction, or by the mere transitory improvement on the part of the patient.

The more acute the lesion and the greater the toxæmia of the patient the smaller should be the initial dose; in the case of the more chronic lesions a considerably higher (2 to 10 times) initial dosage may be safely used. When the blood and lymph supply to an affected part is poor, as for instance the skin and cornea, still higher doses are advisable.

### General References to Vaccine Therapy.

A questionnaire answered by 1261 physicians showed only 17 thought vaccine therapy generally useful for treating infectious diseases; 140 reported harm from stock vaccines; and 17 cases of asthma followed use of vaccines in patients hitherto immune.—L. Hektoen and E. E. Irons, *J. Amer. med. Ass.*, 1/1929, 868.

**Vaccines compared with antiseptics.** The antiseptic method was largely employed in the war, but it made the wounds no better—every microbe

multiplied. Staphylococci and streptococci remained behind after perpetual irrigations with hypochlorite. Government might, with advantage, forbid antiseptics. Optochin, though it will kill pneumococcus in 1 in 400,000 dilution in serum, did not give striking results in practice. Flavine, though not killing the white corpuscles instantaneously, does so on slight "cooking." The Profession is therefore thrown back on vaccine therapy. Vaccine therapy should be used in incipient and localised infections and in septic wounds.—Sir A. Wright, *Brit. med. J.*, ii/1930, 735; *Lancet*, ii/1930, 960. In conditions in which the body is sensitised, *e.g.*, exophthalmic goitre, gouty conditions, and asthma, vaccines should not be used.—Sir W. Willcox, *ibid.*, 962.

On vaccine therapy and immunisation *in vitro*.—Sir Almroth Wright, *Lancet*, ii/1931, 225, 277, 334.

No proof exists of the therapeutic value of vaccines.—D. Embleton, *Brit. med. J.*, i/1931, 355.

Antigen therapy is now entirely empirical, but it would be foolish to suppose that we have seen the limits of the method of active immunisation.—Sir T. Horder, *Lancet*, i/1932, 170.

A belief in vaccine therapy has been one of the greatest delusions of a generation. In chronic infections they can do actual harm.—J. W. Linnell and C. Hoyle, *Practitioner*, ii/1936, 209.

**Doses.** The *prophylactic* doses indicated under the several vaccines in the following pages are suitable for adults in the majority of cases. The *intervals between doses* should usually be 7 days, and may sometimes be extended to 14 days with advantage; in some cases, *e.g.*, whooping cough, when the vaccine is given during the incubation stage of the infection, the intervals should be much shorter—2 or 3 days.

In *treatment*, as regards dose it is a safe rule to follow that the more acute the infection and the more "toxic" the patient the smaller the initial dose. The doses stated are sufficiently small except possibly in severe generalised infections with marked toxæmia, in which perhaps the dose may be halved. As regards intervals there is no general rule, but the smaller the dose the shorter should be the interval between doses. Thus in septicæmic cases where minimal doses are employed these may be required daily or every other day. Clinical signs, and the focal and general reactions afford the necessary guidance. The simultaneous use of a combination of organisms does not entail reduction in doses of the constituents.

#### Doses for Children.

Under 3 years, $\frac{1}{2}$ adult dose.	From 7 to 10 years, $\frac{1}{2}$ adult dose.
From 3 to 7 years, $\frac{1}{2}$ adult dose.	From 10 to 14 years, $\frac{1}{2}$ adult dose.

**Detoxicated Vaccines** (*Genatosan Ltd., Loughborough*). Thomson evolved the idea of treating bacteria, *e.g.*, the gonococcus, with an alkaline solvent, whereby the stroma or bacterial protoplasm and the toxic endotoxin are dissolved. On treatment with acid or acid salt the stroma is again precipitated, the idea being that the toxin is in the solution—the latter is rejected and the bacterial substance, after washing and suspending in slightly acid medium, is used therapeutically.

**Dissolved Vaccines G.L.** (*Glaxo Laboratories, London*). Bacterial cells in solution, a solution of sodium lauryl sulphate 0.025% being the solvent. The surface tension is also reduced, the sodium lauryl sulphate being absorbed by the toxins which are therefore liberated slowly, allowing the production of an adequate supply of antibodies. They are free from reaction and can be given in initial doses of  $\frac{1}{4}$  to 1 ml. for adults and  $\frac{1}{4}$  ml. for children, subsequent doses in both cases being 1 ml. The following are made: acne and staphylococcus, cold (prophylactic and curative), gonococcus, mixed influenza, staphylococcus, streptococcus, anti-typhoid-paratyphoid, whooping-cough (prophylactic and curative).

**Sensitised Vaccines** (*Sharp & Dohme, London*). *Syn.* SEROBACTERINS. Vaccines which have been treated with the corresponding antisera prior to their use.

**Immunogens** (*Parke, Davis, London*). A series of antigens of high activity and relative freedom from bacterial cells and toxins. The following are made: Gonococcus (combined), pertussis, pertussis (combined), pneumococcus, pneumococcus (combined), streptococcus, streptococcus (combined), streptococcus (arthritis).

A type of antigen based upon washing off 24-hour agar growths of the organism with normal saline, agitating to make a homogeneous suspension, and centrifuging. The antigens obtained in the washings are found to be more potent than broth filtrates. The toxic principles are left behind, the washed bacteria being practically as toxic as before treatment. Intramuscular injections thought to be best. Promising reports in connection with streptococcal, pneumococcal and gonococcal infections are forthcoming. Initial dose of the most useful concentration is 0.5 ml. with rises to 2 ml. or more.—Sir T. Horder and H. S. Ferry, *Brit. med. J.*, ii/1928, 177.

**Criticism of Immunogens.** Detoxicated and defatted vaccines found to be clinically inert.—Geoffrey SHERA, *Brit. med. J.*, ii/1928, 360, 1243.

**Residual Vaccines (Autogenous).** The vaccines are washed in combination with hydrogen peroxide.

Of 360 cases, covering a wide range of infections, 294 (81.5%) were successfully treated.—C. E. Jenkins, *Brit. med. J.*, i/1928, 340.

**Phylacogens** (*Parke, Davis, London*) are filtered, sterilised (72 hours) cultures of pathogenic micro-organisms, preserved with phenol 0.5%. The following phylacogens are supplied. Pneumonia, rheumatism, gonorrhoea, erysipelas, and "mixed infection" (suggested for the treatment of all infections, acute or chronic, in which the condition is not due to a specific micro-organism). Nephritis is a contraindication to their use subcutaneously. Intravenous injection is contraindicated in nephritis, in arteriosclerosis, and in cases with severe and dangerous cardiac involvement. The initial dose should always be given subcutaneously.

**Undenatured Bacterial Antigens** (*Lilly, London*) *Syn.* U.B.A. Represent the natural antigenic complexes of the bacterial cells, are free from metabolites and other non-specific elements and constitute efficient immunising agents. They are standardised on the basis of their nitrogen content. The following are made: Acne mixed, coli mixed, gonococcus, pertussis, respiratory, staphylococcus, streptococcus.

### **Local Immunity in Infectious Diseases.**

The description of the mechanism of immunity given on page 923 assumes that any change in immunity is generalised throughout the body. Besredka claims that certain tissues have a very low resistance to certain bacteria, though the other tissues may be able to deal with them easily. Hence, he argues, if the weak tissues be immunised the whole animal becomes immune to the infective organism. Thus he claims that the skin is the weak spot in the case of anthrax, staphylococcus, etc., infections, and the gut wall in typhoid, dysentery, etc. If these are immunised by local treatment then the animal becomes immune. He also says this is not accompanied by the formation of antibodies in the circulation.

A large number of cases of infections localised in the skin or in the bone, including furunculosis, osteitis, osteomyelitis and various infections, have been treated successfully with antibacterial dressings. In the majority of cases the filtrate of the broth culture was employed. (This is supposed to justify the theory that vaccine therapy should be based not on antibody production, but by direct vaccination of the receptive cell, but unfortunately for the theory similar results can be obtained with plain broth.)

A study of the use of dysentery vaccine *per os* was undertaken by the Medical Section of the League of Nations, and comprised the vaccination of 29,880 refugees in camps in Greece. As a result not one person contracted the disease, and in those regions where dysentery was epidemic this method of vaccination had completely stopped the epidemics.

Gratia repeated Besredka's experiments, and finds that though his facts are partly correct, his explanation is very doubtful. He considers the most likely interpretation is that when the bacilli are injected into the skin they are able to multiply and give off their toxic properties, to which the animal reacts by forming immune bodies. Besredka's hypothesis of local immunity is not in agreement with observed fact.—*Per Brit. med. J. Epst.*, ii/1924, 72.

**Antiviruses.** Substances of microbic origin capable of local vaccination without the introduction of antibodies. They are selective in their action, and affect only a certain group of cells known as "receptives," e.g., the staphylococcus vaccine has a selective affinity for cells of the skin and certain mucous membranes. Oral vaccination against typhoid is now taking its place in ordinary practice. *Antivirus dressings* soaked with filtered cultures in bouillon (or a mixture of lanolin and soft paraffin incorporating the antivirus) left in place for 24 hours have been successfully used in a variety of staphylococcal and streptococcal infections, and in many ocular affections, e.g., blepharitis, conjunctivitis, ulceration of the cornea and keratitis.—Besredka, *per Med. Annu.*, 1931, 393. See also *Brit. med. J.*, i/1927, 1020; E. C. Plummer, *ibid.*, ii/1927, 46.

**ANTIVIRUS THERAPY.** Besredka's idea that cuti-immunity can be produced by applying cultures of the organisms to the skin, or by using broth filtrates. Inhibitory power non-specific, but therapy is specific.—R. F. Hunwicke, *Pharm. J.*, ii/1930, 359, *Lancet*, ii/1929, 771.

Anti-virus results in this country not the same as on the Continent.—*Brit. Med. J.*, ii/1930, 142.

**Antipeol** (*Medico-Biological Laboratories, London*). Ointment prepared from vaccine filtrates for immunising and cicatrising treatment of sores, burns, and cutaneous infections.

**Antivirin Brand Products** (*Glaxo Laboratories, London*). Sterile detoxicated filtrates of bacterial cultures, including Staphylococcus Antivirus Liquid, Streptococcus Antivirus Liquid, Mixed Antivirus Jelly (staphylo and strepto), *B. acne* Mixed Antivirus Jelly, Antivirus Nasal Jelly (*M. catarrhalis*, etc.)

**Bacterial Antigen Jels** (*Lilly, London*). Dissolved bacterial proteins in a water-soluble jelly base, for local application in various affections, e.g., Colo-Jel, Ento-Jel, Staphylo-Jel, Strepto-Jel.

**Mastan** (*Napp, London*). Bacterial autolysate of selected strains of strepto-, pneumo-, and staphylococci, and of influenza and tubercle bacilli. It is rubbed into the scarified skin of the upper arm (bleeding in drops must be avoided) as in vaccination, preceded by a tolerance test inoculation, 3 to 10 vaccinations being given in 5 to 10 weeks. The more intense the reaction, the more success is ensured. In neuralgia, acute and chronic inflammation, erysipelas, acne, furunculosis, etc. Contraindicated in open or occluded tuberculosis of the lungs or other organs.

**Bacteriophage.** F. W. Twort in 1915 described the fundamental characters of the filter-passing lysin—or virus—associated with different bacteria. It was shown that it infected bacteria and could be transmitted from culture to culture. Two years later d'Herelle, of the Pasteur Institute, gave the name "bacteriophage" to the contagious filter-passing material causing bacterial lysis.

The bacteriophage can only be propagated in living bacterial cultures, and is a product of bacterial growth rather than of bacterial disintegration.

Action of bacteriophage upon bacteria may be summed up as follows: Exposed to the action of bacteriophage many bacteria become phagogenic; grown in presence of bacteriophage the virulence of many organisms is altered,

and the cultural properties of the bacteria and the character of solid colonies may also be altered; the antigenic properties of bacteria may be modified by the bacteriophage and the bacteria are killed and lysed. Organisms most sensitive to the bacteriophage are members of the typhoid-dysentery-colon group, less susceptible organisms, including diphtheria bacillus, plague bacillus, the bacillus of hemorrhagic septicaemia, staphylococci, streptococci and the cholera vibrio. Variation in virulence is a marked characteristic. It is extremely stable to heat and chemical reagents. Also possesses antigenic powers and various antibodies can be obtained by appropriate manipulation. While d'Herelle holds it is an ultramicroscopic living organism capable of preying on living bacteria, others hold that it is a ferment or catalytic agent, and Kateshuma suggests name "Ferment d'immunité bactériolysant"—*J trop Med (Hyg)*, 1926, 323.

Ultramicroscopic filter-passing bacteriolytic agents represented by bacteriophage of d'Herelle. Nature, conditions favouring bacteriolysis, culture media, and properties—F W Twort, *Lancet*, ii/1930, 1064.

Polyvalent bacteriophage—*Lancet*, ii/1929, 621.

D'Herelle's views on immunity. Many disagree with him profoundly—*Brit med J.*, ii/1930, 563. Bacteriophage theories—*Lancet*, i/1931, 79.

Bacteriophagy is a general phenomenon possibly involving all bacteria—D'Herelle, per *J Amer. med Ass*, ii/1931, 448.

Although a great variety of diseases have now been treated, the results have been so contradictory as to suggest that "once again a vaunted remedy is undergoing the slow and painful process of discredit." It has even been shown, for example, that the phage may be present spontaneously in the urine at some period of the most acute urinary infections. It is clear that the idea of the phage as a kind of bacteriostatic antiseptic for destruction of bacteria *in vivo* is incorrect—*Lancet*, ii/1932, 198.

Continued investigations support d'Herelle's view that they are separate, self-multiplying, particulate organisms. Andrewes and Elford have found that the diameter of the smallest bacteriophage yet examined is identical with that of the virus of foot-and-mouth disease, and the largest is stopped by a filter of such coarseness as to suggest that its particles are within the range of microscopical detection. Bacteriophages can be inactivated by methylene blue in the presence of oxygen and on exposure to light, which is a further point of correspondence between these substances and viruses—*Ann Rep med Res Coun, Lond*, 1931-2, *Brit med J.*, i/1933, 528.

The phenomenon of Twort-d'Herelle and its significance—E Wollman, *Lancet*, ii/1935, 1312.

**Bacté-Phages** (*Anglo-French Drug Co., London*). Therapeutic bacteriophages for oral and topical administration, e.g., Bacté-Intesti-Phage for intestinal affections, Bacté-Dysentery-Phage for acute bacillary dysentery, Bacté-Pyo-Phage for purulent affections.

**Bacterial Antigen Lysates** (*Lilly, London*). Solutions of specifically (bacteriophage) dissolved (lysed) bacterial proteins for local and parenteral use, e.g., Colo-Lysate (combined), containing *B. coli*, streptococci, staphylococci and pneumococci proteins, Ento-Lysate, *M. catarrhalis*, pneumococci, *S. aureus* and streptococci, Neiso-Lysate, gonococci, *B. coli*, *S. viridans* and staphylococci, Staphylo-Lysate, Strepto-Lysate, etc.

**Billivaccines** (*La Biotherapie, Paris, Roberts, London*). A series of vaccine preparations in tablets and pills for oral administration. To be taken fasting before breakfast.

**Enterofagos** (*Continental Laboratories, London*). Polyvalent intestinal bacteriophage. For intestinal affections.

## SERA

**Therapeutic Sera** may be either antitoxic or antibacterial, according to whether they are produced in response to injections of bacterial toxins or of suspensions of bacteria.

In the preparation of antitoxin the antigen used is either the specific toxin or, more usually, the toxoid, i.e., toxin which has been incubated for 4 to 6 weeks at 37° after the addition of 0.2

to 0.4% of formaldehyde. This is injected subcutaneously into the animal, *e.g.*, the horse, with strict aseptic precautions. If unmodified toxin is used it is usually at first mixed with antitoxin, or the animal has a large protective dose of antitoxin given before the inoculation is started. Some reaction, rise in temperature and malaise may occur. Further injections are made at intervals. The quantity injected is gradually increased, and subsequently the injections may be intravenous. The blood is removed from the animal, by the aid of a large sterilised canula, from the jugular vein; 6 to 12 litres may be collected in sterile flasks. The clot is allowed to form by standing 24 to 48 hours, and the serum is decanted into sterile bottles after the addition of a suitable preservative, *e.g.*, 0.3% of cresol or 0.5% of phenol. Concentration of the antitoxin is effected by fractional precipitation. The antitoxins are precipitated with the globulins by half-saturation with ammonium sulphate.

In the *preparation of antibacterial sera* the antigen used is generally a suspension in normal saline of killed bacteria, and is injected intravenously, sometimes suspensions of live bacteria are used.

**Antiviral Sera**, used in the prevention and treatment of virus infections such as measles and poliomyelitis, are usually obtained from the serum of convalescent patients, though they can, in a few instances, be produced artificially in animals.

**Some Limitations of Serum Therapy.** Certain types of bacteria, *e.g.*, the streptococci and *B. coli*, are only general names for very numerous families, and the antibodies efficient against one member may be altogether without effect on another member of the family. Polyvalent sera have been used with some success, but many failures may still be ascribed to this difficulty. Further, the added immunity in the use of a serum is limited in kind and extent. The serum may be deficient in certain necessary properties, *e.g.*, may not be sufficiently anti-endotoxic. Again, the serum may render the patient hypersensitive to future injections of serum from that animal from which the antiserum was prepared. To guard against this it is necessary to inquire before use whether and when the patient has been previously treated with an antiserum.

**Serum Normale (B.P.C.).** *Syn.* NORMAL HORSE SERUM.

Normal serum is obtained from healthy horses. The blood is withdrawn from the jugular vein and, after it has clotted, the serum is collected, a preservative is added, and the serum filtered through a bacteria-proof filter. The product is tested for sterility and for freedom from toxicity.

*Dose.*—150 to 300 minims (10 to 20 ml.).

**Uses.** It is employed locally, internally and subcutaneously in the treatment of hæmorrhage from wounds, etc., the bleeding of hæmophiliacs, and for hæmorrhage from gastric and duodenal ulcers. For the latter it is given orally 3 or 4 times daily, directly after food, in  $\frac{1}{2}$  ounce of water. 60 or 80 ml. may be given in 24

hours. The serum must be fresh—if it does not produce a good reaction in 24 to 36 hours it is useless for the purpose. Those who have previously received an injection of horse serum may be hypersensitive to it. Symptoms, which may include urticarial eruptions, œdema and other signs of anaphylaxis, usually appear 8 to 14 days after treatment but may appear in a few hours. They may be prevented by injecting adrenaline solution.

Burns well treated with normal horse serum. First bathe the part in warm normal saline, remove devitalised tissue, spray with serum containing 0.35% of cresol, and cover with rubber tissue. Good end-results without scar.—S. R. Monteth and R. O. Clock, *J. Amer. med. Ass.*, 1/1929, 1176.

Repeated doses of BCG emulsion in saline produce a state in the sensitised animal which protects it from the anaphylactic shock due to horse serum. With the desensitising, or shocking, dose much in excess of the fatal dose, the protection becomes less effective. Single small doses before or after sensitisation do not induce the state of protection against serum shock.—E. M. Fraenkel and R. J. V. Pulvertaft, *J. Lab. clin. Med.*, 1936, 21, 364.

**Antilusin** (Allen & Hanburys, London) "A" for use *per os* (dose—10 ml. in milk or water 1 to 3 times daily directly after meals) and **Antilusin "B"** for local application are preparations of normal serum.

**Byno-plasma** (Allen & Hanburys, London) contains 1 drachm of sheep's plasma in every ½ ounce. For use in convalescence and debility. Dose.—½ to 2 drachms.

**Hemostyl** (Bengué, London) Fresh hæmopoietic horse serum. In ampoules for oral administration, or as a syrup.

### Thromboplastin.

This name is applied to a substance, derived from blood-platelets, blood cells or tissue cells, which initiates the changes that lead to the formation of the blood clot. According to Howell, thromboplastin acts by liberating prothrombin from combination with an "inhibiting substance"; in the presence of calcium ions the prothrombin is then converted into thrombin and this in turn acts on fibrinogen, converting it into fibrin, the solid substance of the blood clot. Thromboplastin contains the phosphatid cephalin (kephalin); it is soluble in ether, but insoluble in alcohol and acetone. In solution or in solid form cephalin slowly loses its power of hastening the clotting of blood.

Preparations containing thromboplastin are used as hæmostatics for local application to bleeding surfaces. Sterile preparations may be injected subcutaneously or intramuscularly.

Impure cephalin may be prepared from the brains of cattle by macerating in alcohol, pouring off the alcohol through muslin and extracting the residue with ether in the cold. The ether extract is removed, clarified by filtration and evaporated to dryness. The residue contains impure cephalin. Another method is to extract the brain substance, after desiccation *in vacuo* with light petroleum, and to precipitate the cephalin with an excess of acetone. The precipitate, after extraction with acetone and then with alcohol, is dried, treated with ether, and the ether solution evaporated to dryness.

May also be made by chopping up and extracting fresh ox brains with an equal amount of normal saline, leaving in the refrigerator 48 hours, pressing through cheese-cloth and adding to the extract thus made, after diluting with half its volume of normal saline, 0.3% cresol.

Coagulant hæmostatics should be applied locally at body temperature and the wound should not be allowed to cool; keep, if possible, at 37.5°. Application of hæmostatics by continuous irrigation is inadvisable. Coagulen, thromboplastin, cephalin, protagulin, Hemoplastin and fibrogen amongst those reported upon.—J. W. Pickering and A. Hemingway, *Brit. med. J.*, 1/1926, 1029.



**Clauden** (*Luitpold-Werk, Munich; Medical Laboratories, London*). The hæmostatic principles from fresh pulmonary tissue. Administered orally (2 to 4 tablets morning and evening), subcutaneously, intramuscularly or intravenously (10 ml once to 3 times a day); rectally (20 to 30 ml by drip enema), or as a dusting powder. In the treatment of all forms of hæmorrhage.

**Coagulen-Ciba** (*Ciba, London*). Described as a physiological hæmostatic derived from normal bovine blood platelets, supplied as a powder mixed with sugar to ensure ready solubility, and also in 3% solution in ampoules. May be sterilised by boiling. Administered intramuscularly, orally, or locally (3 to 5% solution), may be given very slowly intravenously in emergency. *Dose*.—Up to 20 ml. of 3% solution.

Successful use in a case of typhoid with intestinal hæmorrhage.—L. C. D. Irvine, *Lancet*, ii/1925, 918.

In two cases of hæmoptysis and one of hæmorrhage Coagulen-Ciba 5 g in 200 ml. of water was given with good results in ounce doses every 2 hours.—R. W. G. Stewart, *J. R. nav. med. Serv.* Jan., 1926, 64.

In a severe case, hæmoptysis arrested by intrapulmonary injection of Coagulen.—A. J. Morland, *Lancet*, i/1925, 1238, 1257.

**Hemagulen** (*Lilly, London*). A physiological hæmostatic prepared from fresh brain substance. For topical application to capillary hæmorrhages.

**Hemoplastin** (*Parke, Davis, London*). Solution of prothrombin and thrombokinase for use as a hæmostatic. *Dose*.—2 ml injected subcutaneously and repeated every 4 to 6 hours until hæmorrhage controlled.

**Hirudin**. *Syn.* LEFCH EXTRACT. An active principle from leeches, obtained by treating the minced heads with warm normal saline. *Dose*.—Intravenously, 0.02 to 0.3 g in 50 ml of normal saline. Solutions must be freshly prepared. It has the property of maintaining blood in a fluid condition—1 mg may be dissolved in 0.25 ml of normal saline for the purpose—this quantity will prevent 7.5 ml of blood from coagulating without otherwise altering its composition.

European leeches are varieties of *Hirudo medicinalis*. *H. quinquestrata*, the five-striped Australian leech, is used in Australasia.

## TOXINS

The toxic products of the bacterial growth, either in an albuminous medium or in a medium which is protein-free. The former clearly contains the products of metabolism of the protein-containing medium, while the latter contains only the toxic excretions of the bacteria and small amounts of endotoxin liberated by autolysis.

Diphtheria toxin in dilute solution is used diagnostically in the Schick Test. Scarlet fever streptococcus toxin is similarly employed for the Dick Test.

Toxins from the tetanus and diphtheria bacilli and from staphylococci are converted to toxoid by formaldehyde, and are then suitable for producing active immunity, being less toxic than the unaltered toxins.

## THERAPEUTIC USES OF BACTERIAL PRODUCTS

*The various vaccines, sera, etc., described in the following pages are classified as far as possible under the diseases in connection with which they are used.*

### Acne.

The acne bacillus may alone be the cause of acne, especially of the non-pustular forms; in the majority of cases, however, it is associated with a staphylococcus.

**Acne Bacillus Vaccine** is indicated in the above cases where comedones are the principal features. Combination with polyvalent staphylococcus vaccine may be advisable.

*Initial dose.*—5 millions; then increasing doses—a final dose of 500 millions may be wanted. The interval between doses is 7 to 10 days.

Vaccine treatment seldom of value in acne punctata. Autogenous better than stock vaccines.—H. G. Adamson, *Lancet*, 1/1925, 401.

**Acne Bacillus and Staphylococcus Mixed Vaccine** is prepared from both these micro-organisms in various proportions. Some convenient ratios are the following quantities in each ml. Acne 5 millions with staphylo. 100 and 250 millions; acne 10 millions with staphylo. 250, 500, 1000 and 2000 millions; acne 20 millions with staphylo. 2000 millions.

*For cultivation of the bacillus and preparation of vaccine see Vol. II. For possible endocrine cause of acne and treatment with gonadotropic hormone see this Vol., page 781.*

**Anti-Anthrax Serum.** *Syn.* SERUM ANTICARBUNCOSUM (*FE VIII*), SUERO ANTICARBUNCOSO.

An antibacterial serum prepared by the immunisation of horses, mules or asses with cultures of *B. anthracis*. *FE VIII* states preferably from the horse.

Human anthrax is not a common disease in Great Britain. Three clinical forms are recognised. A malignant pustule may appear in the skin or in the alimentary canal, or the bacilli may be inhaled and infect the lungs. Serum is more useful in the cutaneous form; recovery from the alimentary and pulmonary forms is rare.

**Sclavo's Anti-Anthrax Serum**, obtainable in 10-ml. tubes, (from the Jenner Institute for Calf Lymph Ltd., Battersea) is prepared by immunisation of asses at Siena in Italy.

*Dose.*—In three or four different parts of the skin of the abdomen, injections of 40 to 80 ml. are given at one time. After 24 hours, if there has been no improvement either in the general or local condition, further injections of 40 to 80 ml. are to be made and repeated next day if necessary. *Begin treatment early.*

Rise in temperature following the injection is favourable. Sometimes a rash develops 3 to 8 days after, with or without febrile symptoms; it is unimportant. The serum keeps for 2 years in the dark—a slight deposit is negligible.

For intravenous injection in severe cases 10 ml. or more repeated after 2 or 3 hours if necessary.

Official figures up to the year 1929, supplied by the Factory Department of the Home Office, London, show that percentage mortality from serum treatment only was 6.6, compared with 11.5% for excision only, 11.8% for excision and serum, and 56.8% with no special treatment.

Preparation of anti-anthrax serum from horses or mules by prolonged intravenous immunisation with capsulated strains of *B. anthracis* cultivated on serum agar. Antibody is associated with euglobulins.—A. Sordelli, C. Harsipe and P. Beltrami, *C.R. Soc. Biol. Paris*, Nov., 1923, 1423.

Mortality from malignant pustule (a variety of external anthrax) reduced in Italy to 5.3% since the introduction of treatment by anti-anthrax serum.—*Brit. med. J. Epit.*, 1/1926, 42

Anti-anthrax serum alone, *i.e.*, without surgical excision of the local lesion, is the treatment of choice. 50 to 100 ml. are given intravenously, and the injections continued daily until temperature drops to normal. It is best to begin with 50 ml. normal saline solution containing 5 drops of serum. Also of value prophylactically in 10-ml doses subcutaneously—A. E. Hodgson, *Lancet*, 11/1928, 594.

Anthrax treatment. Serum 80 to 300 ml. as a preliminary, repeated until temperature is normal. "606" in dose of 0.9 g. daily for 3 days, and a fourth dose after a week. Large doses advised.—C. G. Brentnall, *Lancet*, 11/1930, 1174.

Fatal case of anthrax. Eusol fomentations and Sclavo's serum used—A. L. K. Rankin, *Lancet*, 1/1931, 407.

**Bronchitis and Pulmonary Catarrh.** The bacteriology of bronchitis is broadly speaking the same as that of the common cold, except that there is yet no evidence of a virus infection. The predominant organisms in their order and occurrence are.—

<i>B. influenzae</i>	present in 40%	<i>M. paratuberculosis</i>	present in 23%
<i>Pneumococcus</i>	" " 52%	<i>B. Friedlander group</i>	" " 7%
<i>Streptococcus</i>	" " 53%	<i>B. septus</i>	" " 2%
<i>M. catarrhalis</i>	" " 72%	<i>Streptothrix</i>	" " 3%

(Sputum to be examined after washing out the mouth and throat, and expectorating into a sterile bottle immediately on waking.)

The marked relative absence of *B. septus* is notable. The infections of the lower passages are commonly mixed ones. The *pneumococcus* may be regarded as a frequent cause of bronchial catarrh and the most dangerous to the patient. Note also that *B. influenzae* may be resident in the bronchi or pulmonary cells without giving localised though marked constitutional symptoms. The sputum voided may be almost *nil*.

The nature of the infection can best be ascertained by the examination of a stained film of sputum. If this examination is omitted and the sputum is simply placed on a medium like blood-agar, then, in a considerable proportion of the cases, the influenza bacillus, which is probably the most common infection, will be completely missed.—A. Fleming and G. F. Petrie, "Recent Advances in Vaccine and Serum Therapy," 1934

Bronchitis is pre-eminently suited for vaccine therapy—old age and a desperate condition of the patient are not contraindications to treatment

Autogenous vaccines are more likely to be efficacious than stock ones, and it must be remembered that variation in the flora is liable to occur during the progress of immunisation, hence repeated examination is necessary

### Catarrh, Nasal and Tracheal (the "Common Cold").

The organisms principally involved—either singly or mixed—in setting up acute catarrhal infections of the respiratory tract are the *B. influenzae*, *pneumococci*, *B. septus*, *streptococci* and *M. catarrhalis*, and possibly *staphylococci*. The organisms appear in cycles. Thus *B. septus* may be found in 80 to 90% of the cases in each epidemic for 2 or 3 successive years and then disappear altogether for 4 or 5 years.

Common colds may be caused by filtrable virus. Observations were made over a lengthy period of the flora of the respiratory tract of a sample of the community, and the findings compared with the incidence of respiratory diseases. In the winters 1925-6 and 1926-7 there was an increase of respiratory diseases in Manchester, but whilst in the former there was little or no "flu," in the latter

there was. There is some evidence that "flu" is produced by indol-producing hæmophilic bacilli.—*Rep. publ. Hlth med. Subj., Lond.*, No. 57, 1930; *Brit. med. J.*, ii/1930, 569. The organisms may be secondary.—Prof. A. Fleming, *Brit. med. J.*, ii/1930, 736.

Common cold infection due to filter-passing virus incapable of growing on known culture media.—John J. Abel Fund, *Lancet*, ii/1930, 1192.

Chimpanzees are very susceptible to colds closely resembling the human disease, and can be infected with filtrates of nasal washings from human cases of "colds." Colds following inoculation with filtrates are associated with changes in bacterial flora of nose and throat; pneumococci and *B. influenzae* become more numerous.—Dochez, Shibley and Mills, 1930.

In the present state of knowledge it is surely reasonable to grant that a cold may be caused either by a virus or by bacteria, or by both. This is the only hypothesis which can be reconciled with the fact that the average person has two or three colds every year. What disease is there, caused by a single specific agent, recovery from which confers immunity for no more than a few months?—Leader, *Brit. med. J.*, ii/1933, 831.

"The Common Cold," by D. and R. Thomson. A digest of some 2000 papers.—*Brit. med. J.*, i/1933, 754

Vaccines for colds, bronchitis, etc., are usually prepared from mixtures of the micro-organisms commonly involved (*vide supra*).

Mixed vaccines containing some or all of the micro-organisms commonly found in infections of the respiratory tract are used for the treatment and prophylaxis of the common cold, bronchitis, influenza, etc. There is considerable variation in the composition and doses of the vaccines used, and, for treatment, the composition of a vaccine may have to be altered to suit prevailing conditions, e.g., when one particular micro-organism predominates in an epidemic.

*Dose.*—For prophylaxis, which is best attempted in late autumn or early winter, three doses of a mixed vaccine are usually given with an interval of 6 or 7 days between each dose. The first dose may be from 100 to 250 millions of the mixed organisms, and the second and third doses may be respectively twice and four times the initial dose.

For treatment smaller doses must be used—from  $\frac{1}{10}$  to  $\frac{1}{2}$  of the prophylactic dose. The more acute the attack, the smaller should be the dose of vaccine. Injections may be repeated at intervals of 3 or 4 days. The earlier treatment is begun the better.

Mixed vaccines of respiratory organisms have proved of value not only in the treatment of catarrhs, acute and chronic, but also in pulmonary phthisis where bronchitic symptoms are conspicuous—in such cases where staphylococci or streptococci are the secondarily infecting organisms they should be included in the vaccine used.

**Micrococcus Catarrhalis Vaccine.** A vaccine prepared from *M. catarrhalis* alone is of service in nasal, tracheal and bronchial catarrhs, both acute and chronic, in bronchitis and bronchitic asthma and in catarrh of the middle ear, when the causal relationship of this organism to the attack has been demonstrated.

Initial dose of 10 millions may be repeated in 5 to 7 days. In chronic cases 1000 millions or more may be ultimately necessary.

*M. catarrhalis* is one of the constituents of the combined vaccine for colds (see above). *M. catarrhalis* infections may begin at any part of the respiratory

tract—characteristically with an inflamed feeling of the fauces and nasopharynx.

Chronic tracheal catarrh is frequently due to infection by this organism or *M. paratuberculosis*, to which secondary infection by staphylococci, streptococci, pneumococci, and other organisms may be added, or by the pneumococcus alone. Cultivations from the trachea showed that non-gram-staining cocci are present in 78% of normal throats and 68% of catarrhal throats.

*M. catarrhalis* is frequently concerned in the causation of common colds, and of influenza, bronchitis, and pneumonia. Causes very irritable cough with scanty viscid expectoration. It grows best on blood-agar, and produces no acid in glucose broth. *B. septus* causes a mild pharyngitis with painful throat, muscular pain, with, however, no temperature and little or no nasal catarrh—probably a common cause of stiff neck and muscular rheumatism. *B. Friedlander* occurs in many acute and chronic colds, and may cause very profuse coryza.

**Directions for taking secretion for preparations of an autogenous vaccine.**

If in the throat, the mouth is washed out in the morning, the throat gargled, and the teeth washed with sterile water; the patient spits once into a sterile bottle. If, on the other hand, the infection is in the nose, the entrance to the nostrils should be washed with soap and water and the discharge blown into a sterilised bottle, or better, post-nasal swabs should be taken.

*See also* Influenza and Pneumonia.

Anti-catarrhal vaccine evidently of value as patients come regularly in the autumn for a dose.—H. H. Mills, *Brit. med. J.*, ii/1930, 735.

For a period of two years every second child admitted to a home for small children in Stockholm was inoculated with anti-catarrhal vaccine obtained from the State Medical Institution and prepared from strains isolated from patients in children's hospitals and other institutions. Three injections at weekly intervals were given. There were 122 treated children and 125 control children. More than half the number were under observation for three months or longer. No difference in the two groups was found regarding the number of children taking infections, the number of recurrences, the interval between the illnesses, the duration of treatment necessary, or the frequency of complications.—C. Gyllensward, *Acta pædiatr., Stockh.*, 1935, 17, Supp. I, 78.

Autogenous vaccines exerted no influence on the incidence of attacks in 67 individuals suffering from frequent and severe attacks of coryza. A reduction in severity of attacks is the most that can be expected.—L. Hoyle, *Brit. med. J.*, i/1933, 997.

**Kaltron** (Bayer-Meister-Lucius, Leverkusen, Saccharin Corporation, London) Polyvalent cold vaccine. 1 ml. contains *B. influenzae* Pfeiffer 400 millions, streptococci 80 millions, pneumococci 200 millions. Prevention of colds, influenza and catarrh.

### Oral Cold Vaccine.

A combined vaccine prepared by separately growing Pfeiffer's bacillus, pneumococci (types I to IV), streptococci, and *M. catarrhalis* in broth cultures in bacterial symbiosis with *Anaeromyces bronchitica*; when taken for 4 doses ranging from 10 to 20 ml at weekly intervals, produced in the blood, after the fourth dose, agglutinins for pneumococci in 1 in 40 dilution and for streptococci in 1 in 80 dilution, thus indicating a definite agglutination response after oral administration. No toxic symptoms were observed with these doses at weekly intervals, and it is suggested that this weekly oral dose (swallowed, on an empty stomach, before retiring) can be kept up all the winter without any trouble.—D. Thomson, R. Thomson and E. T. Thompson, *Brit. med. J.*, i/1936, 261.

In a group of 445 persons oral administration of vaccine reduced the incidence of cold by 43.7% as compared with the control group.—Rockwell and Van Kirk, *Science*, ii/1935, 178.

**Anepidem** (British Drug Houses, London). Polyvalent vaccine prepared from the mutation forms of the *B. coli communis*. Ampoules of 1 ml. for intramuscular injection or discs for oral use. Treatment of colds, influenza, etc.

**Entoral (Lilly, London).** An oral cold vaccine consisting of killed bacterial cultures of pneumococci (25,000 million), *H. influenzae* (5000 million), streptococci (15,000 million), *M. catarrhalis* (5000 million). *Dose*.—1 capsule with a drink of cold water an hour before breakfast for 7 successive mornings and 2 capsules each week throughout the season.

**Genora Cold Vaccine (Genatosan, Loughborough).** Vaccine for oral administration containing 2000 million organisms per ml., including *B. influenzae*, *M. catarrhalis*, *Anaeromyces bronchitisca*, with pneumococci and streptococci. *Dose*.—10 ml to commence with, taken in water on an empty stomach at bedtime, increasing to 15-20 ml. if there is no reaction. Then 1 dose a week for two months. For the prevention of colds, influenza and pneumonia and for treatment of bronchitis and post-influenzal cough.

**Cerebrospinal Fever.** *Syn.* CEREBROSPINAL MENINGITIS, MALIGNANT PURPURIC FEVER, PETECHIAL FEVER, SPOTTED FEVER.

A diplococcus, *Diplococcus intracellularis meningitidis* Weichselbaum, has been isolated from the cerebrospinal fluid, and from the brain membrane and the purulent exudate. Four serological types of the meningococcus are known, designated by Gordon's classification types, I, II, III and IV, and serum is usually prepared by immunising horses to all four types.

Griffith's Group I corresponds to Gordon's Types I and III, and Group II corresponds to Gordon's Types II and IV. It has been shown that the meningococcus possesses "rough" and "smooth" variants; "rough" cultures are likely to be less potent antigens than smooth, freshly isolated cultures.—C. G. Rake, *Proc. Soc. exp. Biol.*, N.Y., 1931, 29, 287, G. F. Petrie, *Brit. J. exp. Path.*, 1932, 380, and B. G. Malgraath, *ibid.*, 1933, 227.

**Serum Antimeningococcicum (B.P.C.).** *Syn.* MENINGOKOKKEN-SERUM (P.G. VI).

Obtained from the blood of horses immunised to strains of the *Diplococcus intracellularis meningitidis* Weichselbaum, formerly known as *Neisseria meningitidis*. P.G. VI requires a titre of 1 : 100 in complement deviation test, and at least 1 : 1000 in bacteriotropic tests. 2-, 4- and 8-fold strengths are also mentioned.

*Dose*.—10 to 30 ml by intrathecal or intravenous injection.

A dose of 30 ml or more (except when less than this amount of cerebrospinal fluid can be removed) should be given *intraspinally* by lumbar puncture at the earliest possible moment, and repeated daily for at least 4 days. The amount of the dose should be less than that of the cerebrospinal fluid withdrawn, and the serum should be warmed to body temperature and injected by the gravity method. In children under 5 it is inadvisable to give more than 10 ml. In severe fulminating cases the dose if possible should be 45 ml. After the injection the patient should lie with head and shoulders low and pelvis raised. It is also used intravenously, and, in severe cases, intracisternally. Details of method of administration are given in the *Memorandum on Cerebrospinal Fever*, published by the Ministry of Health, 1931.

Serum given early often shortens the illness and reduces the occurrence of complications. It must be admitted that, especially of late years, serum therapy has apparently at times been ineffective. In Detroit (U.S.A.) in the outbreak of 1928-29, there was a fatality rate of 50%. Norton and Gordon conclude that either the local strain of meningococcus was of exceptional virulence or that the therapeutic sera employed were lacking in the appropriate antibody. During epidemic times it is important to arrange for the determination of the prevalent types of the organism and to take steps for the inclusion of fresh representative

types in the immunising doses that are used in the preparation of the serum.—Fleming and Petrie.

Cerebrospinal meningitis in Bombay. Treatment with intrathecal injections of anti-meningococcal serum of the Lister Institute reduced period of illness, prevented the chronic lesions and types of infection, resulted in complete restoration of health in all but a small number of the recovered, and greatly diminished fatalities.—P. T. Patel, *Lancet*, ii/1928, 541.

Streptococcal meningitis successfully treated by intrathecal injection of anti-meningococcal serum.—C. W. Vining and H. P. Thompson, *Brit. med. J.*, ii/1924, 667.

Influenzal meningitis. A case recovered under anti-meningo serum intravenously and intraspinally. Influenza bacillus found in cerebrospinal fluid. Only three cases of recovery on record.—J. Gibbens, *Lancet*, i/1931, 291.

In spite of overcrowding, epidemic meningitis is much less frequent in the Navy than in training depots ashore, due to seamen becoming immunised by contact with carriers of *N. meningitidis* in the training depots.—S. F. Dudley, *Lancet*, i/1931, 511.

Specific univalent serum in preference to multivalent.—H. Stanley Banks, *Lancet*, i/1931, 747.

For earlier references to clinical use of the serum see Vol I, 20th Edn

**Ferry's Meningococcus Antitoxin.** Each of the four types of meningococcus forms, in young broth cultures, a soluble exotoxin which is type specific and also a toxin which is common to all four types. These toxins can be detected by a skin reaction following intradermal injection into the human skin. An antitoxin can be produced in the serum of the horse which is capable of eliminating the skin reaction of the toxin. Experimentally produced cerebrospinal meningitis in monkeys can be cured by intraperitoneal injection of the antitoxin.—N. S. Ferry, J. F. Norton and A. H. Steele, *J. Immunol.*, ii/1931, 293; also N. S. Ferry, *ibid.*, ii/1932, 315, 325, and i/1934, 133.

Treatment of 86 cases with Ferry's antitoxin gave mortality rate of 23.5%, compared with 45.9% for cases treated with anti-meningococcus serum. Doses of 20 to 40 ml. intraspinally, 60 to 100 ml (in twice as much normal saline) intravenously, and repeated daily if necessary, are recommended.—A. H. Hoyne, *J. Amer. med. Ass.*, i/1935, 980.

Ferry's meningococcus antitoxin appears to be a potent therapeutic agent for types I and III meningococcus meningitis, as shown in a recent small series in London. Its potency in type II meningitis is much more doubtful. It is suggested that intensive dosage, viz., twice daily spinal injections in the early acute stage, combined with one or more intravenous injections, is an important factor in the success of treatment. The usual conditions of storage of meningococcal serum in hospital may in some cases be responsible for failure in treatment meningococcal serum ages very quickly and ought not to be used more than 5 or 6 months after collection. Cases treated in London: 7 deaths in 25 cases. Initial dose 15 to 25 ml. intraspinally and 80 to 150 ml intravenously, followed on the next day by similar doses intraspinally and intravenously and 15 to 20 ml. intracisternally, repeat on third day—other doses intrathecally or intravenously if necessary.—H. S. Banks, *Lancet*, i/1935, 856.

Active immunisation with meningococcus toxin. By not less than three subcutaneous injections of Ferry's meningococcus toxin, a certain percentage of individuals who give a positive skin test can be immunised. The immunity to one type can be produced by injection of a mixture of toxins of all types.—N. S. Ferry and A. H. Steele, *J. Amer. med. Ass.*, i/1935, 983.

### Cholera.

The disease is marked by the presence of the *Spirillum cholerae*.

**Anti-Cholera Vaccine.** *Syn.* CHOLERA VIBRIO VACCINE. As an immunising agent only.

**Dose.**—1000 million followed in 7 days by 2000 million. The

first dose may be followed by constitutional disturbance, local redness, pain and swelling of the corresponding lymph glands, effects which should pass off within 3 days. The second dose will probably produce less reaction. An alternative method is to give 3 doses, 500, 1000 and 1000 or 2000 million respectively, allowing intervals of 7 to 10 days between the doses. Full immunity is reached about a week later and persists for 6 months to a year.

The prophylactic vaccines of Haffkine, which have been used with success in India, are prepared from a growth of the spirillum, the virulence of which has been increased by growth in the peritoneal cavity of guinea-pigs. They are:—

(1) Weak. (2) Strong. The dose of these preparations is 1 ml. The second is injected 3 to 5 days after the first (the weak) one. They have to be freshly prepared

A new anti-cholera serum prepared by immunising horses with the toxin obtained from the filtrate of an 18-hours' broth culture of *V. cholerae*. Report of 230 cases treated—H. Ghosh, *Brit. med. J.*, 1/1935, 56.

It is stated that 11·8% of alcohol will kill the *Cholera vibrio* in 4 hours or less, and that 7·8% will cause its disappearance in 1 day. B. B. Brahmachari, per *J. Trop. Med. (Hyg.)*, 1/1927, 225.

Cholera and entero-colitis antiviral orally gave favourable results.—Prof. Besredka, *Lancet*, 1/1929, 1092.

**Bacteriophage.** Under grants from the Royal Society and the Indian Research Fund Association, extensive field experiments have been carried out since 1929 by Lt.-Col. J. Morison and Drs. E. M. Rice and B. K. Palchondbury, on the treatment and prevention of cholera by means of bacteriophage. In Nowgang, in the province of Assam, with a population of half a million, the deaths per 10,000, subsequent to distribution of bacteriophage in 1929, were, for 1930, 0·99, for 1931, 0·78, for 1932, 0·46; for 1933, 0·36. The lowest previously recorded rates since 1906 were 1·34 in 1918, 1·42 in 1920, and 1·62 in 1923. There was no recorded period in which the death rate for four consecutive years compared with those for 1930-1933. In an epidemic in Darrang (an adjacent district) the mortality of the group treated with bacteriophage was only half that of the untreated when the bacteriophage was administered within 24 hours—*Indian J. med. Res.*, April, 1934, per *Brit. med. J.*, 11/1934, 29. See also *Lancet*, 11/1930, 647, *Brit. med. J.*, 1/1928, 365.

### Anti-Colon Bacillus Serum.

**Dose.**—10 ml. or more. Is prepared from horses which have been immunised against a number of types of *B. coli*, principally from cases of peritonitis and puerperal fever.

The action of this serum is chiefly bactericidal, though it also possesses antitoxic properties.

In acute *B. coli* infection of the kidney, Dudgeon has advised 25 ml. of the serum daily for 3 days, combined with calcium lactate to avoid rashes, joint pains, etc.; better in his opinion than vaccines.

Investigations on *B. coli* showed conclusively that these micro-organisms vary in each host; and that probably there are many species which exhibit the same microscopical and cultural appearances.

**Colon Bacillus Vaccine** is used in the treatment of post-surgical suppuration in abdominal cases, such as sinuses which refuse to heal after operations upon the appendix, gall-bladder,



kidney or intestines; also in bacilluria complicating tubercular cystitis, in the nephritis of pregnancy and in endometritis, when due to infection by *B. coli*. Initial doses of 5 million organisms may be repeated at intervals of 7 to 10 days, and may be gradually increased till 100 millions or more are being given. If the doses employed cause any disturbance of the general conditions, as evidenced by rigors or rise of temperature, this must be taken as indication either of pus under pressure or if not this, for diminished subsequent dosage.

Discharging sinuses should, if possible, be kept open, as closing is likely to result in rigors and severe constitutional disturbance.

Immunisation of the patient 3 to 4 days prior to abdominal operations in cases where the presence of pus is suspected is to be advocated—for this purpose a dose of 500 millions may be employed.

In cases of bacilluria the urine should be kept well alkalised by full doses of sodium citrate or sodium bicarbonate.

Vaccine treatment of *B. coli* infections of the urinary tract is practised with generally favourable results.

**RHEUMATOID ARTHRITIS** treated by *B. coli* vaccine intravenously, 50 to 200 millions for first dose, with patient in hospital. Rise in temperature a few hours after injection (100° or 103°F.) Subsequently up to 500 million or more given. The method thought, at least, to be an adjuvant to more recognised methods — R. J. Perkins and C. B. White, *Brit. med. J.*, 1/1923, 411.

See also Peptonum, for non-specific therapy with *B. coli* vaccine.

**Colitique** (*Astier, Paris, Wilcox, Jozeau, London*). Suspension of killed *B. coli* for oral administration, 1 ampoule of 3 ml. contains 3000 million killed bacteria. *Dose*.—Contents of 1 ampoule in a wineglass of water daily before breakfast. Pyelitis and *B. coli* infections generally.

**Antitoxinum Diphthericum** (*B.P., U.S.P. XI*). *Syn* SERUM ANTIDIPHThERICUM (*P.G. VI, P. Ital. V, F.E. VIII, P. Belg. IV, etc.*).

Diphtheria antitoxin consists of the serum, or of a preparation of the serum, containing the antitoxic globulins separated from coagulated blood of the horse immunised by inoculation with diphtheritic toxin, contained in the sterile filtrate from a culture of *C. diphtheriæ* in broth—a surface growth is important. Repeated injections during 4 to 6 months of increasing quantities of toxin, up to as much as  $\frac{1}{2}$  or 1 litre, render the serum of high antitoxic quality. When the horse's serum has acquired a sufficiently high antitoxic activity, the horse is bled about 10 days after the last injection and the serum prepared for use as a remedy, and as a prophylactic. It may consist of the serum, either liquid or dried, or of the antitoxic globulins, either in solution or dried. The dried preparations are obtained by evaporation at a temperature not exceeding 40°, or by means of sulphuric acid *in vacuo*, and are more suitable for export. In preparing the solutions the directions given by each maker should be followed.

The potency is determined by biological assay and is expressed in units. Liquid preparations have a potency of not less than 400 units per ml., and solid preparations a potency of not less than 4000 units per g.

*U.S.P. XI* recognises only the solution of the antitoxic globulins and requires a potency of not less than 500 units per ml. *P.G. VI* includes the liquid or dried serum from horses, mules, oxen and camels. Liquid antitoxin from horses and mules must have a potency of not less than 350 units per ml., that from oxen and camels, only 100 units per ml. The latter is mainly used for prophylaxis. Solid preparations contain not less than 5000 units per g.

*F.E. VIII* describes separately the serum and, with a method of preparation, the antitoxic globulins (*Globulinæ Antidiphthericæ*).

The purification is based on precipitating the euglobulin and albumin, and the pseudo-globulin rich in antitoxin remains. Another method consists in adding the specific antigen to an antiserum and obtaining an antigen-antibody complex, which is then split into its two components — *Lancet*, 1/1929, 292.

For further details of standard, unit, and method of assay, see *Vol II*.

It deteriorates rapidly during the first few months after preparation, subsequent rate of deterioration is at the rate of 5 to 10% per annum, if stored at a temperature not above 10°.

**Dose** — For prophylaxis, 500 to 1000 units should be given to contacts as soon as possible after exposure. This will protect for 14 to 21 days. For treatment, not less than 8000 units to be given for any age, larger initial doses, e.g., from 16,000 to 30,000 units, are required when the case has been delayed until the 3rd or 4th day from onset. Warm the antitoxin by standing in water at 40° for 10 minutes. Do not wait for bacteriological diagnosis. Cleanse the skin with ether soap, and inject in the flank or between the scapulæ. In a sense too much cannot be given. Intravenously, 30,000 to 50,000 units for a desperate case (neutralises toxin more rapidly). Up to 300,000 units have been given intravenously — *Brit. med. J.*, 11/1931, 614.

Children require as large a dose of antitoxin as adults.

*Intraperitoneal injection* may be employed in advanced cases when intravenous injections cannot be given.

**Combined use of Streptococcal and Diphtheria Antitoxins.** *Hæmolytic streptococcus* found in throat of 50% of diphtheria cases. *Streptococcus antitoxin* advocated in addition to diphtheria antitoxin — F. Meyer, *Dtsch. med. Wschr.*, 1928, 215.

Combined use of *streptococcus antitoxin* early as means of preventing onset of septic symptoms — F. von Borman, *Arch. Kinderheilk.*, 1/1931, 241.

Bulk of evidence does not confirm value of combined use of streptococcal and diphtheria antitoxins — A. Fleming and G. F. Petrie, "Recent Advances in Vaccine and Serum Therapy," 1934.

Failure of diphtheria antitoxin in some cases may be due to fact that diphtheria is sometimes wrongly diagnosed in cases of febrile angina when staphylococci and streptococci are present as well as *C. diphtheriæ* to which the patient possesses a natural or acquired immunity. — H. Dold, *Dtsch. med. Wschr.*, 1927, 1760.

**Combined Use of Insulin and Antitoxin.** In toxic cases give a preliminary injection of antitoxin intramuscularly; one hour later make a resting blood-sugar estimation, and inject together intravenously (very slowly at 37°) 32,000 to 100,000 units of antitoxin and 20 g. of dextrose in 50% solution; make further blood-sugar estimations at 1, 1½, and 2 hours after, and if the last

figure shows a return to normal give 10 to 30 units of insulin intramuscularly, and subsequently dextrose by mouth or intravenously. Case mortality reduced from 35.9% to 22.5% and noticeable reduction of serum-sickness—E C Benn, E. Hughes, and S. Alstead, *Lancet*, i/1932, 281.

Patients experienced relief from physical distress by combined insulin and antitoxin—H E. de C. Woodcock, *Lancet*, ii/1932, 884.

Significance of sugar tolerance curves and value of insulin in toxic diphtheria discussed by N D Begg and E H R Harries, *Lancet*, i/1935, 480

**Untoward Results—Serum Rashes, etc., with Diphtheria Antitoxin.** Higher potencies are now used than formerly, and rashes, pain, and swelling are usually considered to be less frequent. Calcium lactate is said to relieve the rash, pain, etc. The symptoms of diphtheria serum sickness are fever and rash, usually urticaria or a variety of erythema multiforme. Sometimes more unpleasant effects, namely, pains in joints, tendons and fasciæ occur with fever. Asthmatic patients should receive injections with caution, even as prophylactic. Intense itching, subsequently vomiting, has been cured by  $\frac{1}{2}$  grain of morphine. Adrenaline hydrochloride solution given hypodermically is also useful in controlling serum rash.

Attention drawn to the growing frequency of unpleasant reactions to the injection of diphtheria antitoxin. At one time these reactions were rare, now they occur in 80% of children and 75% of adults. Ephedrine by the mouth is successful in aborting these reactions—one tablet an hour before the injection and one tablet every 8 hours for the next fortnight. For children under 4, tablets containing 0.1 g.; between 4 and 9, 0.2 g., and between 9 and 15, 0.3 g.—P. Paul Levy, *Brit med J.*, ii/1933, 354

**Diphtheria Carriers** are found of all ages and of either sex; the presence or absence of an obvious pathological condition is no criterion for detecting a carrier, or of virulence. The length of carrier life seems to have no effect on virulence—bacilli have been demonstrated to be virulent after 4 to 8 months in the ear and nose of different individuals. Artificial immunisation under certain conditions may increase the number of virulent carriers, especially when only partially carried out in a community.

Of 1680 children with diphtheria, 86 showed hæmorrhages. Prognosis of epistaxis in concurrent faucial and nasal diphtheria is very serious, but epistaxis is not a very grave sign in purely nasal diphtheria or when disease confined to tonsils and conjunctiva—P von Kiss, *Arch. Kinderheilk.*, ii/1933, 193.

The tooth brush as a carrier of virulent diphtheria bacilli. Immersion for 1 minute in a 5% solution or for 5 minutes in a 2% freshly prepared solution of standard lysol found insufficient to kill *B. diphtheriæ* on artificially infected tooth brushes—G H Culverwell and J Graham Forbes, *Lancet*, i/1923, 255

Ichthammol ointment 10% applied to nasal mucosa of carriers. A negative culture is usually obtained after five consecutive days' use—*Per Prescriber*, 1925, 247

**Schick Test in Diphtheria** (introduced by Prof. B. Schick, of Vienna, in 1913). Schick test toxin is injected into the skin to discover whether a person is immune or susceptible to diphtheria. If his blood contains antitoxin, so that he is immune, this antitoxin prevents the injected toxin from causing a skin reaction. If his blood contains no antitoxin, or insufficient for protection, a circumscribed area of redness about  $\frac{1}{2}$  in. or 1 in. or more in diameter (which may not appear until the third day), persisting 7

to 10 days, is produced, and on fading shows superficial scaling and persistent brownish pigmentation.

**Schick Test Toxin.** A standard diphtheria toxin is diluted so that 0.2 ml. contains the test dose. To ensure that the toxin injected is harmless, B.P. requires that when it is diluted 50 times, 0.2 ml. must cause no reaction when injected into the skin of a guinea-pig, but when diluted 25 times, this dose must cause a reaction. Now the test toxin also contains toxoid which produces no skin reaction but combines with antitoxin. Tests are therefore required to ensure that the test toxin contains a normal amount of toxoid, neither unusually large nor unusually small. The first test requires that 1 ml. Schick toxin mixed with 1 ml. of a dilution containing  $\frac{1}{250}$  of a unit of antitoxin, must give a reaction on the skin of a guinea-pig when 0.2 ml. is injected. This test ensures that the amount of toxoid present is not unusually small, for, if it were, a person might appear immune who in fact had a very small amount of circulating antitoxin. The second test requires that 1 ml. of Schick toxin mixed with 1 ml. of a dilution containing  $\frac{1}{100}$  of a unit of antitoxin must give no reaction when 0.2 ml. is injected into the skin of a guinea-pig. This test ensures that the amount of toxoid present is not unusually large, for, if it were, a person might appear susceptible who had a fair amount of circulating antitoxin. The diluting fluid may be either a sterile solution of sodium chloride, so that the diluted liquid is isotonic with the blood, or may be a sterile solution containing 1.5% v/v of a mixture of 57 g. of borax, 85 g. of boric acid and 99 g. of sodium chloride.

**Method of Conducting the Test.** 0.2 ml. of the standardised diluted diphtheria toxin is injected intracutaneously into the left forearm. A similar amount of control, *i.e.*, toxin which has been heated, is injected into the right arm. A flush, sometimes with a deeper red centre, on the site of injection into the left arm, and the absence of an identical flush on the right arm, indicates a positive reaction. This develops in from 24 to 72 hours and is more easily read on or after the third day.

The control test serves to eliminate *pseudo reactions* due to the presence in the test toxin of some substance which is more stable than the specific toxin and which causes reactions in sensitised individuals.

**Immunisation.** Patients who give a positive reaction should be immunised by *diphtheria prophylactic*, of which usually 3 injections of 1 ml. each are given at intervals of 7 to 14 days.

Babies up to 6 months seem to be immune; between the ages of 6 months and 5 years the majority give a positive reaction, and for children within these age limits the test is often considered unnecessary, and the children may be immunised without previous Schick testing. For immunisation one of the several forms of diphtheria prophylactic is used, the doses and the intervals varying with the different forms.

**Allergic Reactions to the Schick Test.** Report of 14 cases and treatment

with 0.5 to 1 ml. of adrenaline chloride solution 1 : 1000. "In view of the rarity of the hypersensitive state, practitioners need not be unduly alarmed, nor hesitate to perform a Schick test where indicated. The worst of the reactions caused some anxiety for a time, but the subjects soon recovered completely —H. J. Parish, *Lancet*, ii/1936, 310

**Diphtheria Prophylactic.** The *B.P.* '32 includes five forms of Diphtheria Prophylactic (*Toxinum Diphthericum Detoxicatum*). A sixth variety (alum precipitated toxoid) is recognised by the *B.P. Add.*

(a) **Diphtheria Toxin-Antitoxin Mixture**, prepared by adding diphtheria antitoxin to a filtrate of a culture on nutrient broth of *C. diphtherie*

(b) **Diphtheria Toxoid** or **Anatoxin**, prepared by treating the filtrate with formaldehyde.

(c) **Diphtheria Toxoid-Antitoxin Mixture**, prepared by treating the filtrate with formaldehyde and adding a small quantity of diphtheria antitoxin.

(d) **Diphtheria Toxin-Antitoxin Floccules**, prepared by adding diphtheria antitoxin to the filtrate in the proportion necessary to produce suitable flocculation, separating the floccules and washing and suspending them in physiological solution of sodium chloride

(e) **Diphtheria Toxoid-Antitoxin Floccules**, prepared by treating the filtrate with formaldehyde and then proceeding as for toxin-antitoxin floccules

(f) **Alum Precipitated Toxoid**, prepared by treating the filtrate with formaldehyde, adding alum in the proportion necessary to produce a suitable precipitate, separating the precipitate and washing and suspending it in physiological solution of sodium chloride.

**Purified Diphtheria Toxoid.** Culture filtrates containing toxins treated with formaldehyde are partially or completely converted into toxoids. The *Ramon flocculation test* being used for assaying strength of the fractions, the "*Langstaff dose*" being the amount of toxin equivalent to 1 unit of antitoxin by this test —A. F. Watson and E. Langstaff, *Biochem J.* 1926, 763

The lethal effects of diphtheria toxin—also tetanus, *B. Welchii*, etc.—can be prevented by mixing the toxin with fine emulsions of olive oil —G. N. Myers, *J. Hyg., Camb.*, 1934, 34, 250.

All forms of diphtheria prophylactic are submitted to a test to ensure freedom from toxicity which consists in injecting 5 ml into each of 5 healthy guinea-pigs, and in seeing that none die within 6 days. Hence, 1 ml., which is the amount injected into a person, must contain less than one-fifth of the fatal dose for a guinea-pig. Further, if any of the guinea-pigs die later than 6 days, a second test is applied in which 1 ml is injected into each of 5 more guinea-pigs. None of these guinea-pigs must die within 30 days. There are also tests to ensure efficiency.

*B.P. Add.* includes the following tests—A quantity not exceeding 5 times the adult dose is injected once or one-tenth the adult dose is injected twice, with an interval of not more than 4

weeks, into each of not less than 10 guinea-pigs. The immunity produced is such that not more than 2 out of the 10 (or 25 % if more than 10 were used) are Schick-positive. For the toxin-antitoxin floccules and toxoid-antitoxin floccules an alternative test is to carry out the above immunisation with prophylactic on not less than 9 guinea-pigs and then to inject each animal twice, at different sites, with one test dose and two test doses, respectively, of Schick test toxin. A positive reaction to one test dose must not occur in more than one-third of the guinea-pigs and a positive reaction to two test doses must not occur in more than two-thirds. This part of the test is carried out not later than six weeks after the single injection of prophylactic or not later than three weeks after the second of the two injections.

Diphtheria toxin-antitoxin, which was the original form of prophylactic used, has been largely displaced by a preparation of diphtheria toxoid. Injections of toxin-antitoxin may be attended with some danger. Some fatalities have been ascribed to freezing of the mixture which destroys the antitoxin, leaving excess of the toxin. The toxin-antitoxin mixture should not be used after exposure to a temperature below 0°. The addition of formaldehyde renders the toxin non-toxic. (The anatoxin is stable for long periods below 20° and resists heating for 1 hour at 65° to 70°.—G. Ramon, *Ann. Inst. Pasteur*, 1925, 1, per *J. chem. Soc. Abstr.*, 1/1925, 339. See also G. Ramon, *Brit. med. J. Epit.*, 1/1924, 44.) It is not advisable to attempt immunisation in patients with advanced heart disease and kidney affection, or those recovering from acute infectious diseases. It is claimed that 70 to 90% of those treated are found to be immune after 8 weeks. From 1 to 5 years is the most favourable age for diphtheria prophylaxis.

#### REFERENCES TO CLINICAL USE OF DIPHTHERIA PROPHYLACTIC.

(a) **Diphtheria Toxin-antitoxin Mixture.** As already stated, this has now largely been replaced by other forms of prophylactic. For references to its use see previous edition.

(b) **Diphtheria Toxoid or Anatoxin.**—*Ministry of Health Memorandum 170/Med.*, Nov., 1932, gives recommendations which are in accord with findings of conference of experts from different countries held in London, in June, 1931, under auspices of League of Nations. Some of recommendations are: At same time as Schick test a test for hypersensitiveness should be carried out by intradermal injection of a small dose of formal toxoid (0.2 ml. of a 1 in 100 or 1 in 200 dilution). Any reaction to this test within 24 to 48 hours should be taken into consideration when deciding method of immunisation. If no reaction greater than  $\frac{1}{4}$  in. and no induration, immunisation may be carried out with formal-toxoid of 25 to 35 L.F. or greater strength in 3 doses at fortnightly intervals. If there is a reaction to the test with diluted formal toxoid, toxin-antitoxin floccules should be used as immunising agent in place of formal toxoid. Immunisation should not be attempted in children under one year. Schick test should be repeated not less than 2 months after last immunising dose. If positive, whole immunising course should be repeated.

In a small number of cases injection of toxoid has been followed by reactions due to hypersensitiveness of the patient to certain proteins contained in the toxoid. These reactions are harmless to healthy persons and are rare in children under five. For older children, test for hypersensitivity by intradermal injection of diluted toxoid—known as *Moloney test* (*Vide Min. of Health Memorandum above.*)

Use of the Moloney test makes it possible to immunise non-sensitive children with toxoid.—R. A. O'Brien and H. J. Parish, *Lancet*, ii/1932, 178.

The Moloney test has been applied to 57 young adults. Results suggest the test is not an accurate index either of liability to or severity of the reactions to be expected in adults after the injection of formol toxoid.—R. Swyer, *Lancet*, ii/1935, 22

Diphtheria, an almost preventable disease, still attacks some 40,000 people every year in England and kills 2000. In a crucial test in the Edinburgh and Birmingham isolation hospitals immunisation virtually abolished diphtheria among the staff and the nurses, constantly and intensely exposed to risk.—W. T. Benson, *Edinb med J.*, May, 1934, 293, per *Brit. med. J.*, i/1934, 1081

The intrinsic antigenic value of anatoxin should be of at least 5 antigenic units—that prepared by the Pasteur Institute is of 8 to 10 units. Initial injection subcutaneously 0.5 ml. After 3 weeks give a second injection of 1 ml., and 15 days later a third injection of 1 ml. to 1.5 ml. (this third injection is not always necessary). All children from 1 to 8 years should be vaccinated. In epidemics inject 1000 units of antitoxin preceded a few minutes by an injection of anatoxin, the second and third injections of anatoxin being given in the usual way. Nearly 300,000 persons vaccinated in France since 1926.—G. Ramon and G. I. Helie, *J. Amer. med. Ass.*, ii/1928, 1033

After the first dose 37% of children Schick-negative—after second dose 95% to 98% Schick-negative.—L. Marten, G. Loiseau and A. Lafaille, *Ann Inst. Pasteur*, ii/1928, 959.

Results in Canada 400,000 people inoculated with toxoid between 1925 and 1927 without any untoward result.—J. G. Fitzgerald, *Ann Inst. Pasteur*, ii/1928, 1089

Diphtheria toxoid (anatoxin) is a better immunising agent than toxin-antitoxin and may safely be employed in immunising adults. A first dose of 0.5 ml. is given, a second of 1 ml., and a third of 1 ml. to 1.5 ml., with an interval of 14 days between doses. If there is a marked "pseudo reaction" in the Schick test, or a history of diphtheria, give preliminary doses of 0.1 ml. to 0.25 ml. of toxoid.—G. F. Dick and G. H. Dick, *J. Amer. med. Ass.*, i/1929, 1903

Diphtheria toxoid used for active immunisation without any undesirable local or general reactions. Sensitivity to toxoid demonstrated by intradermal tests. It should replace toxin-antitoxin.—Keller and Harris, *J. Amer. med. Ass.*, i/1934, 2163.

In animal experiments a higher degree of immunity produced by a dose of formol toxoid in 5 ml. of normal saline than by the same dose in 0.5 ml. saline.—P. Hartley, *Brit J exp Path.*, 1935, 468

"The evidence already available leaves no doubt that the disease and its often fatal consequences may now fairly be called avoidable"—J. Graham Forbes, *Spec. Rep. Ser. med. Res. Coun., Lond.*, No. 115, 1927

(c) **Diphtheria Toxoid-antitoxin Mixture.** Should be employed on a national scale. More economical than treatment.—E. Donaldson, *Brit. med. J.*, ii/1926, 551.

Review of eight years' work in Birmingham. Since 1927 toxoid-antitoxin mixture has been given in 3 doses of 1 ml. each at fortnightly intervals. Only 14 cases of diphtheria have occurred in 58,000 immunised children.—M. Bard and V. Fellowes, *Lancet*, ii/1934, 1181

(d) **Diphtheria Toxin-antitoxin Floccules.** The precipitate formed by mixing toxin and antitoxin in equivalent amounts contains all the specific antigen and antibody in the mixture with little non-specific matter.—P. Hartley, *Brit J. exp. Path.*, 1925-6, 112. Owing to the elimination of much of the non-specific matter, the reaction following injection of floccules is less than that with toxin-antitoxin.

(e) **Diphtheria Toxoid-antitoxin Floccules.** Absolutely safe for immunisation of children.—A. T. Glenny and C. T. Pope, *J. Path. Bact.*, 1927, 587

Immunity after the injection of floccules is said to develop rapidly. Three injections may be needed. Little likely to produce reactions.—*Brit. med. J.*, i/1931, 757.

Rarely produces reaction in adults and practically never in children.—*Lancet*, i/1935, 229.

Satisfactory results obtained in adults.—D. J. Thomas and N. G. Howell, *Lancet*, i/1935, 579.

(f) **Alum-Precipitated Toxoid.** The addition of alum to toxoid to the extent of 0.2% provides a precipitate of high immunising power even in one dose, though it is apt to cause an annoying, but not harmful, reaction. Its use has been enthusiastically adopted in some of the Western and Southern States of the U.S.A., with a high conversion of Schick-positive children to negative after one dose.—*Brit. med. J.*, 1/1934, 1081

The precipitate produced by addition of alum to formol toxoid is used for immunisation against diphtheria in one dose of 0.5 ml or 1 ml

Superior to toxoid-antitoxin in the prevention of diphtheria. It induces immunity more rapidly and is the best antigen in epidemic periods when rapid induction of immunity is essential. The reactions are not more severe than those caused by toxoid-antitoxin. Observations based on treatment of 436 children with alum toxoid and over 7000 with toxoid-antitoxin.—J. C. Saunders, *Lancet*, 11/1932, 1047

Slight and transient induration developed in approximately half of 38 cases treated, and all the children known to be Schick-positive before treatment were negative when tested three months later. The rationale of alum-toxoid prophylaxis indicates that a certain amount of induration at the site of injection is to be expected. If it can be shown that this is transient the method seems to be well worth while, as the delayed absorption appears to have the effect of increasing enormously the antigenic response of the organism.—J. C. Saunders, *Lancet*, 1/1933, 791

One dose of alum-precipitated toxoid rendered Schick-negative 92.4% of 185 strongly Schick-positive children of pre-school age. In another group of 613 children not previously Schick-tested, 96.6% were Schick-negative when tested 2 to 4 months after one injection.—Graham, Murphee and Gill, *J. Amer. med. Ass.*, 1/1933, 1096

No reactions other than an occasional slight induration observed in 135 infants immunised with one dose of alum-precipitated toxoid.—Walker, *J. Amer. med. Ass.*, 11/1934, 227.

Results compare favourably with those following two doses of formol toxoid.—Kelber and Leathes, *J. Amer. med. Ass.*, 11/1934, 478

Alum toxoid is slightly more effective than toxoid containing no alum.—White and Schlageter, *J. Amer. med. Ass.*, 1/1934, 915

By adsorption on aluminium hydroxide the purity of diphtheria toxoid is increased 150 times. Tests on 9000 persons show that the addition of aluminium hydroxide increases immunising power and practically no reaction is produced.—S. Schmidt, *Dansk Tidsskr. Farm.*, 1933, 123, per *Quart. J. Pharm.*, 1934, 152

All of 553 children immunised with a single dose of purified alum-precipitated formol toxoid were protected, whereas of 175 controls, 7 contracted diphtheria.—Leach and co-workers, *J. Lab. clin. Med.*, 1935, 20, 451

Use of alum-precipitated toxoid in diphtheria immunisation.—J. E. Haine, *Brit. med. J.*, 11/1935, 896. Also McNaughten, White and Foley, *ibid.*, 898

Experiments in Hungary with a single dose of alum-precipitated toxoid in the immunisation of 60,000 children, said to confer as great an immunity as that produced by anatoxin (Ramon).—F. Farago, *Amer. J. Hyg.*, 1935, 22, 495.

Injection of 0.1 ml. of alum-precipitated toxoid followed by 0.4 ml. (or less) 3 weeks later, advocated for older children in whom reactions are likely to occur. The small initial dose gives warning if the patient is likely to react to the larger dose of toxoid. 185 children, of whom 20% were over 10 years of age, immunised by this 2-dose method, with only one mild reaction.—Chesney, *Brit. med. J.*, 1/1936, 208

Evidence to show that the 2-dose method gives a better immunity than a single injection representing the same total amount. Of 321 children given one injection only 64% were rendered Schick-negative, whereas of 35 children who received 0.1 ml. and 0.2 ml. 3 weeks apart, all were Schick-negative 15 weeks later.—Parish, *Brit. med. J.*, 1/1936, 209.

For a full account of diphtheria immunisation, etc., see *Diphtheria: Its Ætiology, Distribution and Transmision*, by J. Graham Forbes (1932).

### Dysentery.

The bacteria causing bacillary dysentery are of two main types—the Shiga and Flexner types of *B. dysenteriae*; the former is



prevalent in South-Eastern Europe and Asia, and the latter in Western Europe and North America.

**Serum Antidysentericum (Shiga) (B.P.).** *Syn.* SERUM ANTI-DYSENTÉRIQUE (*Fr. Cx. Supp.* 1920). The serum (or preparation of the serum) of horses that have been immunised to the toxin of Shiga strains of the *B. dysenteriae*.

*For method of standardisation and unit, see Vol. II*

**Doses.**—Preventive, 4000 units subcutaneously; curative, an initial dose of 8000 to 10,000 units intramuscularly on the outer side of the thigh (into the body of the *vastus externus*), repeated daily till improvement sets in. For a grave case, 10,000 to 20,000 units repeated daily if necessary. Some dilute the dose with 150 to 300 ml. of normal saline and give *intravenously*. In any case, it should be given early. Stools are stated to return to normal rapidly in successful cases, but treatment must be continued. Pains and temporary rashes may result, which, however, need not alarm.

In fulminating cases large doses should be given, also magnesium sulphate 1 dr. 3 times daily for the first few days. In bad cases morphine may be needed, and for very severe tenesmus a suppository containing cocaine  $\frac{1}{2}$  gr. and iodoform 3 gr. is useful.

It is stated that while much of the endemic dysentery prevailing in tropical and sub-tropical countries is caused by pathogenic amœbæ, epidemic dysentery due to *B. dysenteriae* occurs all over the world, and this bacillus is also found in asylum or institutional dysentery, in some sporadic cases of ulcerative colitis and in certain forms of summer diarrhœa.

For a report on the serum treatment of bacillary dysentery, see *Lancet*, ii/1929, 626.

**Polyvalent Antidysentery Serum** is prepared by immunising horses to more than one strain—Shiga, Flexner, Sonne and Hiss-Y strains of the *B. dysenteriae*. Only the Shiga antibody can, at present, be assessed in terms of a standard unit.

**ULCERATIVE COLITIS** Believing that the majority of cases of ulcerative colitis are the result of infection with a dysenteric organism, the author has used polyvalent antidysenteric serum in treatment for the past 15 years. After preliminary desensitisation, 20, 40, 60, 80 and 100 ml. of serum are injected intravenously on consecutive days, sometimes a few additional doses of 100 ml. are given. The treatment can only be undertaken safely in a hospital or nursing home, where the patient is under continuous supervision, owing to the possibility of delayed anaphylaxis. If the patient is treated at home 10 ml. of serum should be injected intramuscularly daily for about 10 days good results are sometimes obtained, although less frequently than with intravenous injections. The great disadvantage of treatment with serum is the possibility of a dangerous reaction. An anaphylactic reaction may occur during the injection of serum, but it is occasionally delayed several hours. Prompt treatment with adrenaline, 1 minim of which should be injected every  $\frac{1}{2}$  minute, after an initial injection of 3 minims, until complete recovery takes place, is almost always effective. Rapid recovery is most likely in the early stages, but it is occasionally very striking, even in the long-standing cases. More frequently the serum produces a certain degree of improvement, with the result that other treatment leads to recovery more rapidly than it otherwise would have done.—A. F. Hurst, *Brit. Med. J.*, i/1936, 321.

**Antidysentery Vaccine.** *Syn.* DYSENTERY BACILLUS VACCINE.

*B. dysenteriae* (Shiga) produces in culture a powerful toxin, but the Flexner type does not produce a similar toxin (*see* Vol. II, 20th Edn, p. 552). The presence of this toxin makes it difficult to prepare from Shiga's bacillus a vaccine that can be given in doses large enough to be efficient. From the results which have been obtained by prophylactic vaccines against Shiga's *Bacillus dysenteriae*, there seems to be no doubt that when vaccine is given in sufficiently large doses a considerable degree of immunity results. The extreme toxicity of the vaccine has been countered by combining it with an antitoxic serum or by treating it with chemicals. Both methods seem to furnish a more or less efficient vaccine. It seems likely that the most satisfactory vaccine of this bacillus will be made by treating cultures with formalin.—A. Fleming and G. F. Petrie.

*B. dysenteriae* (Flexner) includes a number of strains that are antigenically different. A stock vaccine should include representatives of all types. Vaccines of *B. dysenteriae* (Flexner) are practically non-toxic.

**Dose** (of Flexner organisms).—For prophylaxis 250, 500, 1000 millions at intervals of 7 to 10 days. Some give two doses only, 500 and 1000 millions. Initial dose for treatment, 5 to 10 millions.

Dysentery vaccine (carbolsed) reduced mortality in East Africa. Work of late P. H. Ross.—*Lancet*, 11/1929, 1284.

**Oral Use of Dysentery Vaccine.** Vaccine *per os* reduced morbidity and mortality from dysentery. Both prophylactically and therapeutically as effective as serum. Of 3600 men treated in the Rhine Army, none contracted dysentery, while 471 cases occurred in untreated men.—Prof. Besredka, *Lancet*, 1/1929, 1092. Criticism by W. F. Harvey, Prof. A. Fleming and others. "Difficult to know what antiviral is"—*Ibid.*, 1093, 1157.

Prophylactic oral vaccine reported on favourably in the case of mental patients in an Ontario institution. Flexner strains isolated from patients were grown in broth for 4 days, the organisms killed by heat, and 10 ml. of the suspension of dead organisms in the broth given orally in place of the evening meal on the first day, 20 ml. on each of the next 3 days, and 40 ml. on the sixth day, with no appearance of reactions or inconvenience.—E. P. James and S. G. Chalk, *Canad. med. Ass. J.*, 11/1933, 40.

The literature on oral immunisation against bacillary dysentery is not so extensive nor so conclusive as that on oral typhoid vaccination. Nevertheless, animal experiments and the available statistical reports of immunisation experiments carried out in humans demonstrate the possible value of this method in the prophylaxis of dysentery.—D. Thomson and R. Thomson, *Med. Pr.*, 11/1935, 133.

For details concerning differential diagnosis of bacillary and amebic dysentery, and other bacteriological data, *see* Vol. II.

**Gas-Gangrene.** For notes on bacteriology, *see* Vol. II.

**Antitoxinum Welchicum** (*B. P.*). GAS-GANGRENE ANTITOXIN (PERFRINGENS).

Prepared from the blood serum of animals immunised by injection of the filtrate from a culture of *Bacillus perfringens* (*Bacillus Welchii*). Used either as unconcentrated or concentrated (globulin) serum, either in the liquid form or dried.

For standard and method of assay, *see* Vol. II.

**Dose**—Prophylactic, 4000 units. Therapeutic, 10,000 to 20,000 units intravenously.

**Uses.** Has the property of neutralising the toxin produced by *B. Welchii*, and is used for the treatment of wounds infected by this anærobic organism; also in acute intestinal obstruction and peritonitis, and some cases of puerperal sepsis (e.g., following attempts at criminal abortion).

**INTESTINAL OBSTRUCTION** Toxæmia in primary acute intestinal obstruction and in peritonitis with obstruction, due to absorption of the toxin of gas-forming organisms, especially *B. Welchii*. Alkaline contents of lower portion of small bowel, when it is paralysed or obstructed, provide requisite anærobic conditions for proliferation of *B. Welchii*. Improvement recorded in patients suffering from peritonitis with paralytic obstruction by treatment with *B. Welchii* antitoxin. In 54 cases of acute intestinal obstruction treated with antitoxin, mortality rate was 9.3%, as compared with 24.8% in cases not treated with antitoxin. In 256 cases of acute appendicitis treated with antitoxin, mortality rate was 1.2% as compared with 6.3% in control cases.—B. W. Williams, *Lancet*, 1/1927, 907; and *Brit. J. Surg.*, 1926, 54.

*B. Welchii* serum of real value when gangrenous bowel has to be dealt with, but of no benefit in straightforward cases of simple obstruction.—D. P. D. Wilkie, *Brit. med. J.*, 11/1932, 545.

**PUERPERAL SEPSIS** Incidence of *B. Welchii* infections during pregnancy and the puerperium, as shown by records of Obstetrical Dept., St. Thomas's Hospital, London. During years 1922-7, of 16 deaths from puerperal sepsis and generalised gas-gangrene, the bacillus was found *post mortem* in 6. *B. Welchii* not present in cervix before delivery nor in lochia after delivery when pregnancy, labour and puerperium were normal, but of 69 cases in which these were abnormal, *B. Welchii* was isolated in 13. Gas-gangrene antitoxin should be given early in all cases presenting circumstances which may lead to generalised infection, without waiting for bacteriological confirmation of the presence of anærobic organisms.—A. J. Wrigley, *Proc. R. Soc. Med.*, 1930, 1643.

Recovery in a case of puerperal infection treated with antistreptococcus serum, gas-gangrene antitoxin and anticol. serum.—F. Ivens, *Lancet*, 1/1929, 606.

Details of a case of gas-gangrene infection in a woman who died during parturition.—J. and P. Adams, *Brit. med. J.*, 11/1931, 1179.

**WOUNDS.** Every crushed or lacerated wound is a potential source of gas-gangrene, especially if contaminated with foreign bodies. Warning signals are sudden high temperature or temperature mounting a degree or two each day, with rapid pulse and, in young patients, rapid respirations and intense pain. Early signs are the toxic appearance of patient, gangrene of lacerated skin and copper colour of wound. Use of polyvalent gas-gangrene antitoxin, together with tetanus antitoxin, advised in all cases showing suspicion of gas-gangrene.—M. Wiseberg, *Canad. med. Ass. J.*, 11/1932, 278.

See also C. H. Fagge, *Brit. med. J.*, 1/1930, 50; and D. C. Corry, *Brit. med. J.*, 1/1931, 219.

**Antitoxinum Œdematiens (B.P. Add.)** GAS-GANGRENE ANTITOXIN (ŒDEMATIENS).

Prepared from the blood serum of animals immunised by injections of the filtrate from a culture of *Clostridium œdematiens*. Used either as unconcentrated or concentrated (globulin) serum, either in liquid form or dried.

For standard and method of assay, see Vol. II.

**Dose.**—Prophylactic, 20,000 units. Therapeutic, 50,000 to 100,000 units.

**Uses.** Is injected in the treatment of gas-gangrene due to *Clostridium œdematiens*. This organism was responsible for about 15% of cases of gas-gangrene on the Western front during the war.

**Antitoxinum Vibrio-septicum (B.P. Add.)** GAS-GANGRENE ANTITOXIN (VIBRION SEPTIQUE).

Prepared from the blood serum of horses that have been

immunised by injections of the filtrate from a culture of the *Clostridium* commonly known as *vibron septique* (also known as *B. œdematis maligni*). Used either as unconcentrated or concentrated (globulin) serum, either in the liquid or dried form.

For standard and method of assay, see Vol. II.

*Dose*.—Prophylactic, 5000 units. Therapeutic, 10,000 to 20,000 units.

*Uses*. *Vibron septique* is another of the organisms responsible for gas-gangrene, and the antitoxin is used for the same purposes as the other gas-gangrene antitoxins

### Gonorrhœa.

**Vaccinum Gonococcicum (B.P.C.).** Prepared from recently isolated cultures of *Micrococcus gonorrhœæ*.

*Dose*.—Opinions differ widely concerning dosage. In acute urethritis and such complications as arthritis, prostatitis, vesiculitis, epididymitis, the initial dose may be 5 millions (or less), and by judicious use of the vaccine the duration and severity of the disease may be materially shortened. In chronic cases larger doses up to 500 millions may be given. The diagnostic dose in cases of arthritis of doubtful origin is 500 millions (*vide* Streptococcus Rheumaticus vaccine)

A series of injections will usually free any case of chronic gleet from the gonococcal infection, although it may not succeed in stopping discharge entirely in all cases owing to secondary infections.

Doses may be repeated at intervals of 7 days, and gradually increased until a maximum dose of 500 million organisms has been attained.

The injection of large doses of gonococcal vaccine usually gives rise to a reaction, which may be local or general. The *local reaction* consists in redness and swelling at the site of injection. The *general reaction* is manifested by a rise of temperature accompanied by increased pain and tenderness in the affected joints (in the case of gonorrhœal arthritis). Both reactions usually subside within 24 hours. The reactions are less marked after small than after large doses, and are absent in cases free from gonorrhœa.

In the acute stages of gonorrhœa and cases of uncomplicated chronic urethritis, provided the disease is localised to the urethra, vaccine treatment is unavailing. Gleet resists ordinary treatment because the prostate is the seat of mischief; if this gland is massaged every other day for a minute or so by inserting a finger *per rectum* all the secretion is squeezed out; consequently, if an injection of silver nitrate 1% or copper sulphate 5% be now given, the prostate absorbs the solution, and a gleet which has persisted for months or years may not infrequently be cured in a fortnight.

Gonorrhœal prostatitis and vesiculitis. Vaccines of value in some classes — A. Campbell, *Brit. med. J.*, ii/1923, 456.

Autogenous vaccine of great value.—Sir W. Willcox, *Lancet*, i/1923, 1314. Autogenous vaccines of higher value than stock vaccines. It does not matter how small a dose is given at first, it can easily be increased rapidly until there are signs that the vaccine is taking effect. In gonorrhœal rheumatism care

should be taken not to increase the dose by too large an amount daily—the regular emptying of the prostatic focus and massage every 5 days the best form of treatment—*May, A. T. Frost, Lancet, i/1923, 1314*

Simultaneous injections of autogenous vaccine (6000 million organisms per ml.) with protein of value in gonorrhœa. Initial dose of vaccine 0.2 ml., increased by 0.1 ml. to 1 ml.—*A. Tansard, per J. Amer. med. Ass., ii/1925, 1433.*

**Arthigon** (*Schering, London*) Polyvalent gonococcal vaccine in a sterile solution of urotropine 40%. Supplied in ampoules of 1 ml., containing doses of from 10 to 1000 million organisms, given either intravenously or intramuscularly.

**Dmelcos** (*Pharmaceutical Specialties (May & Baker) Ltd, London*) A stabilised atoxic vaccine consisting of an emulsion of several strains of the Ducrey bacillus, each ml containing 225 million organisms. It is injected intravenously in the treatment of soft sore and suppurating buboes and, on account of its fever-producing properties, in general paralysis.

**Gono-Yatren** (*Bayer Products, London*). Polyvalent gonococcus vaccine preserved in 3% Yatren solution. Given intramuscularly or intravenously in the treatment of chronic gonorrhœa and its complications.

**Gonoderm** (*Parke, Davis, London*). The bouillon filtrate of the gonococcus grown in liquid culture medium—contains the soluble toxin described by Corbus and Ferry. Used by intradermal injection in the treatment of acute, sub-acute and chronic gonorrhœa.

**Neo-Dmagon** (*Pharmaceutical Specialties (May & Baker) Ltd, London*) Fluorised anti-gonococcal curative vaccine. 1 ml contains 150 million gonococci and 225 million synococci. Given by intramuscular or subcutaneous injection every second day.

**Vaccigon** (*Napp, London*) Polyvalent gonococcus vaccine in 1 ml ampoules containing from 10 to 1000 million organisms.

**Hay Fever Vaccine.** A solution of grass pollen toxin preserved with 0.5% phenol. Prepared by extracting grass pollen by alternately freezing and thawing the pollen in normal saline. Strength stated in "units." 1 unit is defined as the amount of extract yielded by one-millionth of a gramme of pollen. *Immunisation* should be commenced in susceptible persons during February with an initial dose between 20 and 100 units (depending on the degree of susceptibility as shown by the skin test or eye test). Subsequent doses may be given every 7 or 10 days, cautiously increasing the amount each time. If time is short, doses may be given more frequently—several times a day if necessary. *In treatment* the initial dose may be determined by the ophthalmic reaction, or failing this, give 50 units initially.

"Rush" inoculation in hay fever. Injections given every 1½ to 2 hours throughout a 14-hour day. Initial dose ranges from 20 to 30 units to 100 or 200 pollen units, according to severity of diagnostic reaction—*J. Freeman, Lancet, i/1930, 745.*

Extraction of pollen with 0.27% NaHCO<sub>3</sub> + 0.5% NaCl.—*C. Armstrong and W. T. Harrison, Publ. Hlth Rep, Wash., 1925, 1466.*

Extraction with mixture of glycerin (50%) and above salt mixture gives a solution which is less irritating to the tissues—*G. T. Brown, J. Allergy, 1932, 3, 2.*

Extracts from all grass pollens furnish one and the same antigen for the purpose of desensitisation to hay fever. A patient who is sensitive to one grass pollen is sensitive to all. Timothy grass, *Phleum pratense*, is the pollen to which patients are most sensitive, and desensitisation to this pollen desensitises to all grass pollens.—*J. Freeman, Lancet, i/1933, 573 and 630.*

Best method for immunisation is by long succession of prophylactic doses given in the early spring up to the hay fever season, commencing with a small initial dose of 40 units and gradually rising to as much as 10,000 units. If immunisation is commenced in February, a dose every other day will prove sufficient, if in March, a dose every day, and in May, three, four or even five

doses a day. It is always possible to resort to a "rush" course in a hospital, when desensitisation can be completed in a week by cramming eight doses into each day. The most convenient method is to teach the patients to inoculate themselves—J. Freeman, *Lancet*, ii/1936, 92.

For a consideration of cutaneous tests and non-specific protein therapy in asthma, hay fever and numerous allied affections, see p 733 et seq

**Influenza Bacillus Vaccine.** Prepared from killed cultures of the *B. influenza* (Pfeiffer's bacillus).

The influenza bacillus believed by Pfeiffer to be the cause of epidemic influenza must now be regarded as a secondary invader rendered pathogenic by the primary infecting agent, a filter-passing virus. The work of Smith, Andrewes and Laidlaw (1933) on the filter-passing virus of human influenza is referred to in Vol. II, 20th Edn., p. 563.

The organism only occasionally occurs alone, frequently it is accompanied by the *Pneumococcus*, *Streptococcus*, *M. catarrhalis*, or the bacillus of whooping cough. Many cases of so-called "influenza" are due to the *Pneumococcus*, *Streptococcus* and *M. catarrhalis* either separately or together, and in these the mixed vaccines for colds (p. 934) are used. In influenzal septicæmia or endocarditis, the initial dose is 10 to 25 millions, in true acute influenza 100 to 250 millions. Chronic influenza, especially if complicated by sinusitis or antral trouble, may persist for years if untreated, and large doses of vaccine, 1000 millions or more, may be needed for its cure.

There is no danger in giving it during an epidemic of influenza, but those already acutely infected should receive smaller doses, e.g.,  $\frac{1}{2}$  or  $\frac{1}{10}$  the normal. For prophylaxis begin with 100 millions, and follow in 7 days with 250 millions and increase up to 1000 millions

Apparently vaccination with organisms other than the Pfeiffer bacillus has given the same doubtful results in prophylaxis as when mixed strains of the Pfeiffer bacillus have been employed. In view of the doubt regarding the causal relationship between *B. influenza* and the disease influenza it would be well to change the name of this organism to Pfeiffer bacillus.—Stitt

#### War Office Conference Vaccine.

<i>B. influenza</i>	400 millions	} in 1 ml
<i>Streptococci</i>	80 "	
<i>Pneumococci</i>	200 "	

It originally contained 60 millions of *B. influenza*

With the increase in proportion of the first mentioned, the vaccine may prove a powerful reinforcement to measures of protection. Dose— $\frac{1}{2}$  ml. with a further 1 ml. after 10 days' interval. Table of results over wide area—Sir W. B. Leishman, *Lancet*, i/1920, 366.

For notes on the conclusions of the Conference (1918) on vaccine therapy in influenza, see 20th Edn., p. 915.

The treatment of influenza.—Lord Horder, *Brit. med. J.*, ii/1934, 1059

Investigation of influenza epidemic. Photographic records of cultures on Crowe's medium from throat and sputum. Constant presence of a pneumo-like streptococcus.—D. Thomson and R. Thomson, *Lancet*, i/1929, 388

Avoidance of a city area by an institution staff during the pandemic of 1918 resulted in no influenza.—E. A. Rainsford, *Lancet*, i/1929, 635

The apparent identity of the Koch-Weeks Bacillus with *B. influenza* is commented on.—*Lancet*, i/1930, 517

**CONVALESCENT SERUM.** Two cases of influenzal pneumonia treated by intravenous injection of convalescent serum 10 ml. Dramatic recovery in each case—R. Hare, *Lancet*, ii/1933, 293.

**Aplexil** (*Pharmaceutical Specialities (May & Baker) Ltd, London*). Anti-influenza vaccine containing streptococci, pneumococci, Pfeiffer's bacillus and *M. catarrhalis*. Injected subcutaneously for prophylaxis and treatment.

### **Pneumonia.**

**Vaccinum Pneumococcicum (B.P.C.).** Prepared from killed cultures of representatives of all the recognised serological types of the pneumococcus, or from one of the types only.

This vaccine, besides being of service in pneumonia (it should be given early), is also used in empyema, especially in children (in adults, combination with a streptococcal vaccine may be advisable), in nasal and laryngeal catarrh, asthma and bronchitis, periostitis, otitis, endometritis and pyosalpinx, where initial doses of 100 millions may be employed, when due to this organism.

**Dose.**—10 millions initially is repeated or increased at intervals of 7 days, according to clinical symptoms. Cases of delayed resolution in pneumonia are benefited by injections of 50 to 100 millions every 8 to 10 days, while routine treatment of all cases of pneumonia during the first week, by doses of 25 to 50 millions whenever there is a rise in the temperature, has been practised. In pneumococcal eye infections an initial dose of 250 millions is appropriate, and in pneumococcal septicæmia 10 to 25 millions.

It is probable that a large percentage of failures with stock vaccines is due to the vaccine not conforming in type with the infecting organism. Stock vaccines must be polyvalent, and polyvalent in each of the types peculiar to the country. Autogenous vaccines are clearly preferable.

**P.S.I. Vaccine.** Wynn's formula contains per ml 200 millions each of pneumococci, streptococci and *B. influenza*. **Dose**—1 ml (children require smaller doses, e.g. 20 millions of each organism at 1 year—W. H. Wynn, *Brit med. J.*, ii/1934, 1159).

### **Sources of the *Pneumococcus* and Modes of Infection.**

Pneumonia is rarely caused by auto-infection from the germ so commonly present in the throat in health, but is usually due to infection with pneumococci present in the air, dust, etc.

The specific antigenic substance from the pneumococcus is said to be a complex carbohydrate.

The percentage of cases of pneumonia due to bacteria other than pneumococcus is probably very much greater than is supposed. This was verified by the experience of the widespread epidemics in 1918-19 of so-called "Spanish flu." In cases where pneumonia is said to supervene upon influenza, the infection is a double one from the beginning, and much may be done to prevent the pneumonic attack by giving doses of 25 to 50 millions of pneumococcus vaccine, combined with 50 to 100 millions of *B. influenza*, as early as possible during the influenzal attack.

**Prophylactic Inoculation.** Sir A. E. Wright found that doses up to 40,000 million produced nothing more than a slight constitutional disturbance and slight rise in temperature. Lister advises a vaccine of four types containing 6000 millions per ml of each type, making a total of 24,000 million per ml.

Of this 1 ml. is given as initial dose, twice repeated, at intervals of 7 days. Borel holds similar views, and he inoculated Senegalese troops in France with initial doses of 32,000 million without ill effect.

For white races, work of investigators of the Rockefeller Institute shows that initial doses of 1000 million each of the prevalent strains can be safely used, and that with lower doses full immunity may not be secured. After 7 days either 1000 or 2000 million is given, and a further 2000 million 7 or 14 days later.

Free from risk and appears to be of value in many incipient cases of pneumonia.—J. Staveland Dick, *Lancet*, 11/1925, 1110.

**Types of Pneumococci.** Types I and II are the strains most often present in epidemics. They are rarely found in the throats of those who have not been in contact with cases, the normal throat types usually belonging to Group IV.—Stutt, 1927.

Types of pneumococci in relation to disease. Group IV in the eye, nose, and accessory sinuses. In acute otitis media and mastoiditis type III strains and group IV organisms found in about equal numbers.—J. T. Smeall, *Brit. med. J.*, 1/1931, 661.

Immediate pneumococcal typing.—R. R. Armstrong, *Brit. med. J.*, 1/1932, 187. A direct method of typing.—W. R. Logan and J. T. Smeall, *ibid.*, 188.

**Serum Antipneumococcicum I (B.P. Add.)** *Syn.* ANTI-PNEUMOCOCCUS SERUM (TYPE I). Prepared from the blood serum of animals immunised by injections of cultures of *Diplococcus pneumoniae* type I. Used either as unconcentrated or concentrated (globulin) serum, either in the dried or liquid state.

For standard and method of assay, see Vol. II.

**Dose.**—50,000 to 150,000 units intravenously.

**Used** in the treatment of lobar pneumonia when type I pneumococcus is present. As the types of pneumococci (see *antea*) have in general a high degree of specificity, a homologous serum is necessary.

**Serum Antipneumococcicum II (B.P. Add.).** *Syn.* ANTI-PNEUMOCOCCUS SERUM (TYPE II). Is similar to the preceding, except that the cultures used for immunising the animals are of pneumococcus type II.

For rapid methods of typing the pneumococcus, see Vol. II.

Report on treatment of 1375 cases in Aberdeen, Edinburgh, London and Glasgow (1930-1933). Concentrated antiserum for type I reduced fatality between ages of 20 to 40, but had little effect from 40 to 60. Seemed definitely to reduce average duration of fever and illness in patients who recovered, and decreased liability to empyema among survivors. Similar effects seen with type II antiserum in type II cases. A good serum seemed devoid of disturbing effects on patients. Use not recommended except when typing of pneumococcus can be obtained. If typing can be done in 5 or 6 hours, withhold serum till type is known and then give dose intravenously of 20,000 Felton units of the specific serum, but if more time is required give preliminary dose of 20,000 Felton units, type I, with 20,000 type II, and continue specific serum when nature of infection is known. Continue with 20,000 units twice daily at 8-hour intervals with average total of 80,000 units. Useless to continue if no obvious clinical improvement in 48 hours. Make first injection cautiously—1 ml. in a minute or



two and the total in 10 or 15 minutes. If patient reacts unfavourably inject at once subcutaneously  $\frac{1}{2}$  or 1 ml. of 1 in 1000 adrenaline solution.—Report of Therapeutic Trials Committee of the M R C., *Brit med. J.*, 1/1934, 245.

Serum treatment of type I lobar pneumonia—report of 30 cases, 15 of which were treated with concentrated serum—D. Leys, *Lancet*, 11/1935, 748

Serum treatment of pneumonia. There is a strong probability that the use of larger doses of type II serum, which the fear of severe reactions at present makes difficult, would produce as good results as those obtained with type I serum. Early treatment is essential.—D. Leys, *Lancet*, 11/1935, 67

Analysis of cases of lobar pneumonia with early administration of serum. The following phenomena were observed in patients treated with homologous serum during first 24 to 48 hours. Disease may be completely aborted, temperature, pulse and respiration rate dropping to normal within 12 to 24 hours after administration, improvement in general condition due to disappearance of toxæmia; prevention of spread of infection from one lobe to another and limitation of area in lobe primarily infected, prevention or rapid check of bacteriæmia, rapid return of leucocytes to normal—R. L. Cecil, *Brit med J.*, 11/1936, 308

**Felton's Serum.** A polyvalent serum containing immune bodies against type I or type II pneumococcus, or against both. As soon as the diagnosis of lobar pneumonia is made the pneumococcus type is ascertained from the sputum

An intradermal and conjunctival test is first made with a 1 in 10 dilution of horse serum. If, after 15 minutes, the tests are negative, 5 ml. of Felton's serum is slowly injected intravenously, followed 1 to 2 hours later (in the absence of reaction) by 20 ml., and this dose repeated every 2 to 3 hours up to a total of 100,000 units (100 ml serum). Repeat on second day, reducing to half doses if condition is improved, on third day, if temperature is under 100°F and condition is good, give one or two 10-ml. injections to prevent relapse. Benefit is usually apparent after 2 to 3 days' treatment. The results with type I (the most highly parasitic) are excellent, and in type II quite definite—R. L. Cecil, *Brit med. J.*, 11/1932, 657

Mortality of type I infections reduced by more than half, but that of type II little, if at all, affected. No evidence that serum lessens toxæmia, prevents complications or hastens resolution—J. Cowan and co-workers, *Lancet*, 11/1932, 8.

If the organism is found to be type I or II give 20,000 units of the correct type intravenously (after testing for sensitivity). If typing has not been done, give 20,000 units of mixed I and II. Repeat dose 6 to 8 hours later if temperature has not appreciably fallen, if a fall takes place give 10,000 units and increase, repeat (or withhold) 6 to 8 hours later. If sputum is not produced till the third or fourth day, give 20,000 units of mixed serum if infection is thought pneumococcal, repeated at 6 to 8-hour intervals until result is obtained or sputum typed.—A. J. Scott Pinchin and H. V. Morlock, *Practitioner*, 11/1933, 378

### **Snake Bite.**

The chief poisonous snakes belong to the Colubrine and Viperine families. The former includes the cobras, coralline snakes, kraits, hamadryad and the death-adder, the latter includes the rattlesnake, puff-adder, bush-master and copperhead. A serum produced from a Colubrine venom is not effective against the venom of a Viperine snake and *vice versa*. Specificity is also shown by the antitoxins produced from the venoms of individual members of the two families. Polyvalent sera are impracticable owing to the extreme toxicity of mixed venoms.

**Serum Antivenenosum (B.P.C.),** *syn.* ANTI-IVENENE, is a generic name for anti-venom sera. It consists of the serum of

horses immunised by subcutaneous injections of snake venom. The most useful serum for general use is prepared by injecting a mixture of 80% cobra venom and 20% viperine venom

*Dose.*—100 ml. or more intravenously.

### Snake Venoms.

In view of the apparent confusion, it may be useful to summarise the venoms that have been employed therapeutically. Cobra venom has been used as an analgesic, particularly in cancer, this and puff-adder venom in the treatment of epilepsy, moccasin venom has found an application in certain hæmorrhagic conditions and skin diseases. All these are given by injection. Dilute solutions of Russell's viper venom are only employed as hæmostatic applications direct to bleeding surfaces. This venom is probably the most effective local hæmostatic available—R G Macfarlane and B Barnett, *Lancet*, 1/1936, 509

#### Cobra Venom.

**CANCER** Jacques Lavedan has for some two years given injections of cobra venom to patients suffering from various forms of malignant disease. In 51 cases the treatment was continued systematically for at least four months, the cobra venom being introduced either directly into the new growth or at some distance from it, and, broadly speaking, nothing but failure was registered. It is true that considerable relief from pain ensued in some cases, but it could have been obtained more reliably and cheaply with morphine. Histological examination of the tumours supplied no reliable evidence that their vitality had been injured—*Bull Acad Méd, Paris*, 1935, 195

**EPILEPSY** There is sufficient evidence of the successful treatment of epilepsy with snake venom to warrant further investigation. The treatment would, of course, be quite empirical, though reports seem to show it depends on something in the nature of protein shock—B Barnett (Curator of Reptiles, Zoological Society of London), *Brit med. J.*, n/1934, 1073. Dr Burgess Barnett is prepared to advise medical men as to the most suitable form of snake venom for use in any particular type of case, and as to the method of obtaining an aseptic product by appropriate treatment of the venom—R H Elliott, *ibid*

**Venene.** Prepared by F W FitzSimons from puff-adder venom, wight-adder venom, cobra venom and mamba venom, at the Port Elizabeth Museum and Snake Park (S. Africa).

*Dose.*—Initially, for a healthy adult, 5 minims subcutaneously, increased at weekly intervals of 2, 3 and 4 weeks up to a maximum of 40 minims. It is issued in bottles containing 20 ml of a 1 in 300 solution with glycerin 10% and cresol 0.3%.

Used with success in epilepsy.

The Medical Association of S Africa declined a paper by Mr FitzSimons on the treatment of epilepsy by snake venom, and the Editor of the Medical Journal of S Africa refused to publish same on the grounds that there was nothing new in the treatment, and that it could no more be called a cure for epilepsy than common salt is a cure.—*Brit med J.*, 1/1929, 34

The preparation has been widely used for epilepsy in South Africa, and Mr FitzSimons, in a paper read before a combined meeting of the British and South African Associations for the Advancement of Science, in July, 1929, reported encouraging results. There seems to be a *prima-facie* case for investigation of the claims. The benefits claimed may be due to desensitisation—*Lancet*, ii/1930, 915

#### Moccasin Venom.

**HÆMORRHAGE.** Moccasin snake venom given intradermally or subcutaneously has a definite effect in decreasing the permeability of the capillaries, and is of value in hæmorrhagic states other than hæmophilia or idiopathic thrombocytopenic purpura.—S. M. Peck and N. Rosenthal, *J Amer. med Ass.*, 1/1935, 1066.

**MENORRHAGIA.** 7 cases of menorrhagia, in which no organic lesion could be demonstrated, were successfully treated by subcutaneous injections of a 1 in 3000 solution of moccasin venom. Initial dose 0.4 ml, increased by 0.2 ml

at 3-day intervals for the next two doses, when reaction usually occurred and the dose was reduced to 0.05 ml. Subsequent injections at 3-day intervals were increased to 0.1 ml and then 0.2 ml, provided no untoward local reaction occurred. Dose then increased by 0.3 ml. until a dose of 1 ml. could be given twice a week. Injections continued for several months, but improvement usually within 1 or 2 months.—C. H. Watkins, *Proc. Mayo Clin.*, 1936, 261. See also *Venoms and Antivenenes*, a collection of abstracts from recent papers—*Trop. Dis. Bull.*, 1936, 379.

**PURPURA HÆMORRHAGICA.** An intradermal moccasin snake venom test has been used as a prognostic measure in essential thrombocytopenic purpura hæmorrhagica. Persistence of a positive reaction to successive tests, or a reversal to a negative reaction, is of value in determining the trend of the purpuric state. Subcutaneous injections of moccasin snake venom have been employed as a therapeutic measure in chronic purpura hæmorrhagica. It apparently has been of value in 22 of the 34 cases in which it has been used. The effect of subcutaneous venom injections and the trend of the intracutaneous venom test are important for the indication and prognosis of splenectomy.—S. M. Peck, N. Rosenthal and L. A. Erf, *J. Amer. med. Ass.*, i/1936, 1791.

#### Viper Venom.

**HÆMOPHILIA.** The venom of Russell's viper clots hæmophilic blood more quickly than any other venom—one drop of a 1 in 1000 solution added to 10 drops of hæmophilic blood causes clotting in 17 seconds, and a 1 in 100,000 solution in 60 seconds, the clot being tough and firm. The solution is easily sterilised by filtration through a Berkefeld filter; the venom maintains its potency unchanged when dry, but soon deteriorates in dilute solution. Striking results in local hæmorrhages (*e.g.*, from tooth sockets) in hæmophiles, bleeding stopped at once by application of 1 in 100,000 solution.—R. G. Macfarlane and B. Barnett, *Lancet*, ii/1934, 985.

Hæmorrhage in a hæmophilic boy successfully controlled by application of 1:10,000 dilution of Russell's viper venom.—G. A. Baker and P. C. Gibson, *Lancet*, i/1936, 428.

Snake venom and its use in dental hæmorrhage.—J. Draper Cambrook, *Proc. R. Soc. Med.*, 1936, 281.

**Stypven** (*Burroughs Wellcome, London*). Russell viper venom for topical application in the control of external bleeding. It is issued in rubber-stoppered bottles accompanied by hermetically sealed ampoules of solvent consisting of sterile distilled water containing 0.5% of phenol. A solution of the necessary concentration is prepared by adding with a syringe the solvent to the rubber-stoppered bottles. The solution is stable only for a limited period, and should not be used after 7 days.

### Rheumatoid Arthritis.

#### **Streptococcus Rheumaticus Vaccine.** *Syn.* ANTIRHEUMATIC VACCINE.

Prepared from killed cultures of streptococci isolated from rheumatic cases.

**Dose.**—Initial dose, 1 to 5 millions. Subsequently at weekly intervals with a 50% increase each time.

In doubtful cases of rheumatic arthritis a dose of 250 to 500 millions of *Streptococcus rheumaticus* may be given diagnostically, and the temperature observed every 4 hours for 24 hours, a marked temperature or local reaction will assist greatly in establishing the diagnosis.

Extreme caution in the use of this vaccine is necessary. Even 500,000 may cause a most unpleasant reaction, and until the urine is free from organisms more than 5 millions can seldom be given.

Vaccine therapy should never be used until the focus of infection has been removed as far as possible.—Sir W. Willcox, *Brit. med. J.*, i/1926, 1045.

The initial dose should be one million, and after the first three or four doses the increase should be 25 or 50% of the previous dose, the interval between

the first few doses being 3 or 4 days and later a week.—K. Stone, *Practitioner*, 11/1927, 183.

Rapid improvement following subcutaneous injections of *B. fallax* vaccine. *B. fallax* is an organism occasionally isolated from gangrenous wounds and cases of puerperal sepsis. Advisable to add the organism to autogenous vaccines in treatment of chronic arthritis, especially when joints have been damaged previously by injury or are the seat of disease non-pyrexial and insidious from the onset.—J. and N. Mutch, *Lancet*, 1/1927, 1022.

*S. viridans* the commonest organism isolated from rheumatic patients—whether teeth, tonsils, or bowel.—*Lancet*, 1/1929, 1016

A questionnaire sent to all patients treated during the year 1928-9 at the Devonshire Hospital, Buxton, showed that there was no evidence of greater benefit in those treated with autogenous vaccines than in the vaccine group as a whole, and it would appear that vaccines show no better prospect of improvement or cure of infective arthritis than other methods of treatment — P. M. Congdon, *Lancet*, 1/1932, 180

*B. coli* vaccine intravenously in rheumatoid arthritis, see *B. coli*, p. 940

## Septicæmia.

**Serum Antistreptococcicum (B.P.C.).** The serum of horses that have been immunised by injections of streptococci. In the preparation of polyvalent sera, a large number of strains (hæmolytic, non-hæmolytic and *S. faecalis*) are used. They are obtained from a number of infections, e.g., erysipelas, septicæmia, endocarditis, uterine infections, influenza, appendicitis, etc. Some strains of streptococci, e.g., those from scarlet fever, erysipelas and puerperal sepsis, produce toxic culture-filtrates, injection into horses of these toxic products, as well as of the bacterial cultures, yields a serum that is antitoxic as well as antibacterial. The serum may be used without further treatment (natural serum), or the antibodies may be partially purified and redissolved in saline (concentrated serum).

Indicated in simple septicæmia or sapræmia. Erysipelas, endocarditis, carbuncle and acute rheumatism have been treated with it.

**Dose.**—30 ml. early in any form of septicæmia, and repeated every 6 hours if necessary. Injections are made under the skin of the abdomen or flank or at the seat of inflammation, if any as in erysipelas, so as to produce good local effect.

Special antistreptococcic sera for use in erysipelas, puerperal fever, scarlatina, endocarditis and rheumatic fever, are obtainable

There is no standard or unit of potency for polyvalent antistreptococcus serum

**PUERPERAL FEVER** Serotherapy results in puerperal infection are inconstant. Preferably given intravenously in the earliest stages also used locally—50 ml introduced into uterine cavity daily. To prevent acclimatisation of infective organisms large doses (60 to 100 ml) must be given for the first three or four days and the treatment then suspended. In benign cases, vaccines are preferable, but they are useless and even dangerous in profound general depression and asthenia, very acute septicæmia, or with cardiac, renal, or adrenal deficiency. Dose still largely empirical, but preferable to begin with small ones.—*Brit. med. J. Epit.*, 1/1925, 24

Antistreptococcic serum in septicæmia hardly justifiable—serum sickness. An effective method of immunising donors needed.—L. Colebrook, *Brit. med. J.*, 1/1925, 659

Antistreptococcic serum 50 to 70 ml. during labour, or a few days prior to onset, if trouble anticipated. Radiostoleum in addition.—S. J. Cameron and H. Thomson, *Brit. med. J.*, 1/1931, 350

*Streptococcus* septicaemia treated with scarlet fever antitoxic serum. *S. haemolyticus* isolated. Given subcutaneously or intramuscularly, and never more than 20 ml. at a time.—A. B. Rosher, *Lancet*, i/1930, 129.

Morbidity in puerperal sepsis mainly due to a single cause, the *Streptococcus pyogenes*. Vaccines a failure.—R. R. Armstrong and W. Shaw, *Brit. med. J.*, ii/1928, 1084.

**Antitoxinum Scarlatinum (B.P.C.).** *Syn.* STREPTOCOCCUS ANTITOXIN (SCARLATINA), SCARLET-FEVER STREPTOCOCCUS ANTITOXIN CONCENTRATED (GLOBULIN).

An antitoxin prepared from the serum of horses that have been immunised by injection of the toxic culture filtrates of *Streptococcus haemolyticus scarlatinae*, or of the toxin from this organism or by a modification of these methods. There is no international unit for this antitoxin. The potency is sometimes stated in terms of a "unit" based on a skin test on the human subject. The test (which is an application of the Dick Test, *q.v.*) depends upon the fact that injection of the toxin intradermally produces in non-immune subjects a reddening of the skin; if the toxin is mixed with antitoxin before injection this reaction does not occur. The original neutralising unit of the Dicks was the amount of antitoxin required to neutralise one skin dose of toxin. The United States Public Health Service has adopted a "unit" which is 50 times the original Dick unit. Another method of assay (used in Great Britain) is the Parish-Okell rabbit method. 0.25 ml. of a satisfactory antitoxin injected into the vein of a rabbit will protect it against the subsequent injection of 6 ml. of a virulent culture containing the *Streptococcus scarlatinae*. The manufacture of the antitoxin is controlled by patent.

**Dose.**—The absence of agreement regarding a satisfactory "unit" has led to lack of uniformity in statements of dosage; this is variously stated in terms of volume and of the (American) "units" described above, without any direct correlation.

**Dose for treatment.**—10 to 30 ml. (equal to about 300,000 to 900,000 U.S.A. units) according to severity of case; usually establishes normal temperature in 36 hours, and the quarantine period is shortened in many cases by nearly 50%. If given early, it generally arrests the progress of complications and may lessen the severity of complications already developed.

**Dose for Prophylaxis**—5 to 10 ml (150,000 to 300,000 U.S.A. units) for children of 5 to 15 may confer passive immunity for 10 to 14 days.

**Uses.** For the treatment of scarlet fever and the temporary immunisation of contacts; also to distinguish the rash of scarlet fever from other rashes (Schultz-Charlton reaction). *Streptococcus* antitoxin (scarlatina) is also widely used in the treatment of acute streptococcal infections other than scarlet fever, especially puerperal septicaemia.

**Schultz-Charlton Blanching Test for Diagnosis.** 0.2 ml of streptococcus antitoxin (scarlatina) is injected intradermally into the chest, abdomen or forearm, where a uniform scarlet-fever rash not more than 70 hours old is available. A blanching 10 mm

to 40 mm. in diameter appears 4 to 10 hours later, and persists from 12 to 72 hours in most patients suffering from scarlet fever. The antitoxin may be used undiluted or diluted 1 in 10 in normal saline solution—diluted antitoxin should not be used later than six months after preparation.

Treatment of scarlet fever.—A. Joe, *Brit. med. J.*, i/1935, 483.

Specific antitoxin in the treatment of scarlet fever.—A. G. Robb, *Brit. med. J.*, i/1926, 11, *ibid.*, i/1926, 26.

Intravenous antitoxin in scarlet fever. 10 to 20 ml. dose in acute stage stops the acute process in a few hours.—H. S. Banks and J. C. H. Mackenzie, *Lancet*, i/1929, 381; H. S. Banks, *Lancet*, i/1929, 1248.

Control of scarlet fever in a children's hospital.—D. McLean, *Lancet*, i/1927, 483.

Therapeutic results with scarlet-fever antitoxin.—G. F. Dick and G. H. Dick, *J. Amer. med. Ass.*, ii/1925, 1693.

ERYSIPELAS. An antitoxin prepared by immunising horses with several strains (eight) of the streptococcus of erysipelas used in 3311 cases over a period of five years at the Bellevue Hospital, New York, reduced the number of deaths by 30% and reduced the average duration of the disease by 60%, but only of value in controlling the immediate process, and does not prevent additional attacks. It is given intramuscularly in 10-ml. doses, commenced as soon as diagnosis is made, and repeated every 12 to 24 hours for 6 doses, when it is discontinued if no improvement is evident.—D. Symmers and K. M. Lewis, *J. Amer. med. Ass.*, ii/1932, 1082.

PUERPERAL SEPTICÆMIA. Scarletina antitoxic serum used in puerperal septicæmia with mortality 29.6%. In every case *S. pyogenes hæmolyticus* was found.—H. Burt-White, *Lancet*, i/1930, 19.

There is no trustworthy clinical evidence that the administration of anti-streptococcal serum for the treatment of human infections by hæmolytic streptococci has had any specific curative effect. The evidence obtained in puerperal fever cases at Queen Charlotte's Hospital suggests that such administration may sometimes have an unfavourable effect on puerperal infections by hæmolytic streptococci, and in such cases it is best not to interfere with the immunising mechanism of the patient until we can be sure that such interference does not do harm. Until our knowledge of the immunisation against hæmolytic streptococci has progressed further it would seem desirable to discontinue the use of antistreptococcal sera in the treatment (and prophylaxis) of puerperal fever and "surgical sepsis."—L. Colebrook, *Lancet*, i/1935, 1085.

RHEUMATISM, ACUTE. Results from streptococcus antitoxin (scarlatina) compare favourably with those obtained with salicylates. Severe systemic reactions may occur, and this treatment considered suitable only for hospital or institutional patients.—Eason and Thomson, *Edinb. med. J.*, 1934, 41, 583.

**Toxinum Scarlatinum (B.P.C.).** *Syn.* STREPTOCOCCUS TOXIN (SCARLATINA), SCARLET-FEVER STREPTOCOCCUS TOXIN.

The diffusible exotoxin obtained from a broth culture of a good toxin-producing strain of *Streptococcus hæmolyticus scarlatinæ*. The organism is grown in a suitable fluid medium which is then centrifuged and filtered through a bacteria-proof filter. The potency of the toxin is expressed in skin-test doses (S.T.D.). One S.T.D. is the amount required to give, on hypodermic injection, an erythematous zone 10 mm. or more in diameter in the majority of susceptible persons.

The toxin, suitably diluted, is used in the Dick Test for susceptibility to scarlet fever, and also for actively immunising those who are susceptible.

**Dick Test.** The toxin is diluted with normal saline so that 1 S.T.D. is contained in 0.1 to 0.2 ml., and this quantity of toxin is injected *intradermally* (not subcutaneously) into the front of the

forearm, the site having been carefully cleansed. If the patient is susceptible to scarlet fever, a positive reaction will appear, reaching a maximum in 18 to 24 hours and characterised by a circumscribed area of redness, about 1 to 2 cm. in diameter, which persists for a few days and then fades, leaving a brownish pigmentation. The slightest reddening constitutes a positive reaction provided it attains a diameter of 10 mm. Owing to the high dilution of the toxin, pseudo reactions are very rare and a control is unnecessary. The syringe and needle must *not* be sterilised by means of alcohol since this precipitates the toxin; they should be boiled in distilled water.

**Active Immunisation.** *Streptococcus* toxin (scarlatina) produces a more permanent immunity than that conferred by scarlet-fever antitoxin. It is administered subcutaneously or, preferably, intramuscularly. Five injections should be made at 5 to 7-day intervals, the doses being 500, 2000, 8000, 25,000 and 80,000 skin-test doses respectively. In strongly Dick-positive reactors the initial dose may be reduced to 250 S.T.D. In about 10% of cases a reaction occurs, characterised by vomiting, malaise and a scarlatiniform rash. The reaction may occur at any stage of the course. According to the Dicks, the reaction is prevented by administering 2 to 3 m of 1 in 1000 adrenaline solution simultaneously with the toxin.

**SCARLATINAL PROPHYLAXIS BY INHALATION IN ADULTS** The author grew, in glucose broth, the hæmolytic *streptococcus* of scarlet fever, made a suspension of it of a strength of 0.0084 ml in 1 ml of normal saline and heated it for half an hour at 100°. This preparation was given to 11 Dick-positive reactors in an inhaler with a solution containing 1% each of sodium bicarbonate and sodium chloride. The doses of this antigen were 2 ml, 3 ml, and three of 5 ml. at 2 to 3-day intervals. Following this mode of administration 9 of the 11 became Dick-negative, agglutination by their serum took place at titres of 1 in 160 to 1 in 1280. There were no adverse effects—G. Ishiyama, per *Bull. Hyg.*, Nov., 1935, 701.

**Streptococcus Vaccine (Polyvalent).** A polyvalent vaccine prepared from numerous strains of streptococci. (The classification of the streptococci is dealt with in Vol II.) May be employed in localised infections, as erysipelas, lymphangitis, ulcers, sinuses, tonsillitis, adenitis and mastitis; also in asthma and bronchitis, and in generalised infections such as septicæmia and pyæmia, provided the streptococcus has been proved to be responsible. *Initial dose* in very acute and in generalised infections should be 5 or at the most 10 millions, in more chronic conditions a dose of 25 to 50 millions is suitable and may be increased to 100 millions. In erysipelas doses of  $\frac{1}{2}$  to 1 million may be repeated at intervals of 1 or 2 days. In most other conditions the interval between doses should be 6 or 7 days.

*See also Streptococcus rheumaticus vaccine and pyorrhœa alveolaris.*

**PUERPERAL SEPTICÆMIA** well treated with local dressings of gauze impregnated with streptococci, the dressings being changed from three to five times in 24 hours. Not less than three dressings were applied—Per *J. Amer. med. Ass.*, 11/1925, 780.

**FIBROSITIS** In 25 cases of long standing the local injection of a lipovaccine was found of value. The lipovaccine was made up in two strengths, representing

one and ten million organisms (polyvalent streptococci isolated from rheumatic cases) suspended in sterile olive oil, with 1% Gomenol as antiseptic. The oil was injected deeply into the fibrositic area and distributed throughout it by moving the needle, as much as 10 ml. of the stronger concentration used at one sitting. Within a few hours the area became hot and tender, with malaise and evening pyrexia, but all symptoms subsided at the end of a few days, leaving the fibrositic area comparatively painless and a marked gain in general health.—G. Laughton Scott, *Brit med J*, 1/1936, 302

**Strepto-Yatren** (*Bayer Products, London*) Streptococcus vaccine preserved in 3% Yatren solution. Ampoules of 2.5 ml. contain different strengths—25, 50, 100, 200, 250 and 300 million germs. Injections intramuscularly or intravenously in increasing doses at intervals of 2 to 4 days. Erysipelas, abscesses, puerperal sepsis, etc.

### Coley's Fluid.

Contains the combined toxins of *Streptococcus erysipelas* and *B. prodigiosus*. As now prepared is a modification of the original.

**Dose**—Inject a dose daily into tumour, or neighbourhood of tumour, beginning with 0.25 minim into the tumour, or 0.5 minim elsewhere, and if little or no reaction increase by 0.25 or 0.5 minim daily till a rise of temperature to 102° to 104°F is reached. For first few doses dilute with boiled water to ensure accurate dosage. If depression follows injections give at longer intervals. Continue injections till reaction has calmed down and temperature fallen.

**Used** in inoperable cases of malignant disease, especially sarcoma. It has been noted that malignant growths may decrease in size or completely disappear after an attack of erysipelas.

The treatment was not given a fair trial in London, but Coley's claims to cure 10 to 12% of inoperable sarcomas were undoubtedly valid. Three cases saved by it.—J. McNamara, *Brit med J*, 1/1928, 1134.

Cases of lymphosarcoma and Hodgkin's disease respond readily. These diseases should no longer be regarded as absolutely hopeless.—*Ann Surg* Oct, 1928.

### Staphylococcal Infections.

**Antitoxinum Staphylococcicum (B P Add)** Prepared from the serum of horses that have been immunised by injections of the toxin of *Staphylococcus aureus*. It may consist either of the unconcentrated or of the concentrated (globulin) serum, either in the dried or liquid state.

For standard and method of assay, see Vol. II.

**Dose**—Prophylactic, 2000 to 4000 units. Curative, 10,000 to 20,000 units, intravenously or intramuscularly, repeated after 12 or 24 hours.

**Uses.** Although the majority of cases of staphylococcal infection of the skin respond to local treatment with or without treatment with vaccine or toxoid, in some patients a generalised toxæmia or septicæmia may follow. The antitoxin appears to be chiefly efficacious in pyæmic cases. Useful in acute staphylococcal infections and toxæmias so long as the cocci are not detectable in the circulating blood. Few cases of staphylococcal bacteriæmia recover, except when the primary focus is in the bone marrow; treatment with staphylococcal antitoxin should supplement surgical measures, and will sometimes avert a fatal issue.



Prophylactically, it is employed when there is risk of a generalised infection, *e.g.*, from carbuncles, osteomyelitis and mastoiditis, or before operations.

A serum obtained by immunisation of horses, first with toxoid and afterwards with unaltered toxin, given intramuscularly in 104 cases of staphylococcal infection, ranging from carbuncle to septicæmia; as much as 600 ml. may be needed in a severe case. Of 64 patients in whom positive blood cultures were obtained, 29 recovered.—C. E. Dolman, per *Brit. med. J.*, ii/1934, 950.

**Vaccinum Staphylococcicum (B.P.C.).** *Staphylococcus vaccine* is prepared from killed cultures of *Staphylococcus albus*, *S. aureus* and *S. citreus* (mixed vaccine), or from *S. aureus*, or (less commonly) from *S. citreus* or *S. albus* alone.

**Dose.**—Initial, 100 millions, increased to 1000 or even 5000 millions, at intervals of 7 days.

**Used** in the treatment of localised staphylococcal infections, *e.g.*, furunculosis. Often an autogenous vaccine is to be preferred to a stock one.

In cases of acne, *Staphylococcus albus* is commonly associated with the acne bacillus (*q.v.*). In boils, carbuncles, sycosis, ulcers, and sinuses generally, and in acute generalised infections, such as pyæmia, ulcerative endocarditis, septicæmia and in peritonitis, either *S. albus* or *S. aureus* may be found, but *S. aureus* is relatively the more common. The mixed vaccine may, if necessary, be used.

**Staphylococci toxins.** Burnet and Kellaway's investigations.—*Lancet*, ii/1930, 975.

**Neo-Dmesta (Pharmaceutical Specialities (May & Baker) Ltd., London).** Fluorised antistaphylococcal vaccine. 1 ml. contains 450 million staphylococci and 50 million *Micrococci tetragem.* For intramuscular or subcutaneous injection in staphylococcal infections.

**Opsonogen (Chemische Fabrik Gustrow, Gustrow i Meckl.; Braun, London)** Polyvalent staphylococcus vaccine. **Dose.**—100 to 250 million intramuscularly, increasing to 1000 million. Furunculosis and all staphylo-mycoses.

**Propidex (Pharmaceutical Specialities (May & Baker) Ltd., London).** Antistaphylococcal ointment. A mixed vaccine of streptococci, staphylococci and *B. pyocyaneus*, for local application to surface lesions of a pyogenic nature—boils, carbuncles, etc.

**Staphar (Bayer Products, London).** Mixed staphylococcus vaccine. **Dose.**—0.5 to 0.75 ml. subcutaneously or intramuscularly, increasing to 1 ml. 3 times weekly. Staphylococcal infections.

**Staphylosan (Napp, London).** Polyvalent staphylococcus vaccine. Ampoules contain 100, 400, 600 and 1000 million organisms per ml.

**Staphylococcus Toxoid.** The staphylococcus toxin, like diphtheria toxin, can be converted to toxoid by formaldehyde. To a high-potency staphylococcus toxin, formaldehyde is added to give 0.1 to 0.15% *w/w* of HCHO and the mixture incubated at 37° for 14 days.

**Dose.**—0.05 ml., increased to 1.0 ml. at intervals of 7 days.

*Staphylococcus* toxoid may be used instead of the vaccine in the treatment of chronic staphylococcal infections. It is especially useful in severe cases, *e.g.*, recurrent furunculosis, chronic and sub-acute osteomyelitis and in patients convalescing from acute staphylococcal toxæmia.—See C. E. Dolman, *Lancet*, i/1935, 307; also Vol. II, 20th Edn., p. 592.

**Report of the Therapeutic Trials Committee.** Amount of circulating antitoxin readily increased by injections of staphylococcus toxoid, and this is attended with clinical improvement in the majority of cases of furunculosis, but acne does not respond as well as do pure staphylococcal infections. Doses of 0.05, 0.1, 0.2, 0.3, 0.4 and 0.5 ml. at weekly intervals, intramuscularly. Very few reactions noted.—D. S. Murray, *Lancet*, i/1935, 303.

Of 23 cases of sycosis barbæ treated with injections of toxoid, 12 were cured and the remainder much improved. Of 24 cases of staphylococcal infection other than sycosis (mostly carbuncles and boils) 18 were cured and the remainder much improved.—J. I. Connor, *Brit. med. J.*, ii/1935, 1195

Favourable results, with no serious reactions, in treatment of staphylococcal infections of the skin with sterile formalinised filtrates of staphylococcus cultures.—M. A. Gohar, *J. trop. Med. (Hyg.)*, 1935, 259.

Alum precipitation increases potency of the toxoid.—Leonard and Holm, *J. Immunol.*, ii/1935, 209.

Method for the production of staphylococcus toxin and toxoid. Toxoid should contain at least 6 flocculating units per ml. and at least 5 antitoxin-binding units per ml.—Dolman and Kitching, *J. Path. Bact.*, 1935, 137.

Clinical investigation of staphylococcal toxin, toxoid and antitoxin.—Parish and co-workers, *Lancet*, i/1934, 1054

Antigenic efficiency of staphylococcus toxoid should be maintained in respect of leucocidin as well as alpha-hæmolysin.—F. C. O. Valentine, *Lancet*, i/1936, 526

**Staphylococcus Vaccine Toxoid (S.V.T.)** (*Lister Institute, London; Allen & Hanburys, London*). A mixture of staphylococcus vaccine and staphylococcus toxoid—1000 millions staphylococci and 0.5 ml. toxoid per ml. Dose.—0.1 ml., increased to 1 ml. at intervals of 4 to 7 days.

**Staphylococcus Vaccoid** (*St. Mary's Hospital, London; Parke, Davis, London*). A mixture of staphylococcus vaccine and toxoid; issued in two strengths, (a) for children, contains 60 millions of staphylococci per ml. with "weak" staphylococcus toxoid, and (b) for adults, contains 300 millions of staphylococci per ml. with "strong" staphylococcus toxoid. Dose.—0.1 ml., increased to 1.0 ml. at intervals of 7 days

## Tetanus.

### Antitoxinum Tetanicum (B.P., U.S.P. XI)

Prepared from the serum of horses that have been immunised by injections of the toxin or toxoid of *Bacillus tetani* (*Clostridium tetani*); the serum may be used in the liquid state or dried, or it may be concentrated by precipitating the antitoxin-containing globulins which are used either in solution or in the dry state. Liquid preparations for prophylactic use contain not less than 300 units per ml., and for therapeutic use not less than 1600 units per ml. Solid preparations contain not less than 3000 and 16,000 units per g. respectively. U.S.P. XI recognises only the solution of the antitoxic globulins and requires a potency of not less than 300 U.S.A. units (approximately 600 international units) per ml.

For notes on the international unit and assay, see Vol. II.

**Dose.**—Prophylactic, 1000 to 2000 units; therapeutic, 20,000 to 40,000 units.

The Lister Institute advises as follows —

(1) **In Acute Tetanus.** At first sign of tetanus give very large doses energetically and continuously—32,000 to 40,000 international units beneath the spinal arachnoid (in the usual position for lumbar puncture) and the same amount intramuscularly on the outer side of the thigh into the body of the vastus externus

muscle. If no improvement at end of 12 to 18 hours repeat the doses once a day for 3 to 4 days. Later, diminished doses subcutaneously, but patient is not out of danger for a long period

*Warm the serum first to 99° or 100°F. before injecting.*

Rise in temperature with rashes which should pass off.

### (2) *Premonitory Symptoms.*

General restlessness suddenly changing to a desire for rest and *vice versa* Unreasonable outbursts of temper. Increased nervousness. Sleeplessness with distressing dreams and sometimes nightly delirium Temporary giddiness, violent headache, excessive yawning, diffuse backache Trembling of the tongue, which is put out to one side. Some local swelling, without redness, of the injured member and throbbing of its arteries notwithstanding that the limb is raised. Slight jerking may follow pressure on the flexor tendons and increased irritability of the muscles. A profuse sweating, and darting pain in various parts. Difficulty in micturition, due to spasm of the sphincter vesicæ, which may last from a few minutes to half an hour Changes in the facial appearance, the patient looks anxious, though there is as yet no *risus sardonicus* Increased flow of saliva, spasmodic cough Earache, stiffness at angle of jaw Difficulty in swallowing. Tremors and clonic spasms which are not painful and may not attract attention. Pain persisting after muscular contraction induced by effort.

### (3) *Prophylactic Use of Antitoxin and Treatment of Wound.*

*Dose.*—At least 1000 international units to be given *under the skin of abdomen or flank* in every case of injury where possibility of *Cl. tetani* infection If there is soiling of the wound, or there is much dead tissue in a wound which is several days old before observation, give 3000 to 6000 international units intramuscularly 3 to 6 hours before operation if the latter is needed. Use iodine in the local treatment of the wound, as it has strong destructive action on tetanus toxin. Intramuscular injections are preferably given in the outer side of the thigh (into the body of the vastus externus muscle)

*The best results are obtained by intrathecal (intraspinal) injection* at the earliest stage, repeated for 3 or 5 days and supplemented by intramuscular doses. When operating at the site of wounds a prophylactic dose of 1000 i u should be given 2 days before the operation

Prophylactic injection prolongs the incubation period enormously, so that tetanus may occur after wounds have healed. The duration of the complete passive immunity is short, probably not more than 2 weeks after a dose of 1000 units.

**ANAPHYLACTIC SHOCK** The danger of this is negligible when the prophylactic dose is contained in such a small quantity as 2 to 3 ml of horse serum In curative treatment, where massive doses have to be given, the case is different Small subcutaneous doses, rapidly increased, remove risks.—*Lancet*, 1/1917, 105, 114.

Intramuscular route and large doses in tetanus needed, with chlorbutol (15 gr. in olive oil *per rectum*) as a depressant of reflex excitability—D. Bell, *Brit. med. J.*, 1/1931, 75.

Better results obtained by giving large doses (50 to 100 ml.) subcutaneously by the intraspinal route *under chloroform anaesthesia*, ending with subarachnoid injection of 10 to 30 ml. The chloroform impregnates the lipoids of the nervous system, rendering it impossible for the toxins to become fixed—an example of “phylaxis.”—René Cruchet, *Brit. med. J.*, 1/1932, 86.

**Intra-Cerebral Injection** has been practised. The injection must be concentrated and free from antiseptic. A blunt needle is used.

16,000 units injected into the cisterna magna cured tetanus after lumbar route failed.—T. O'Carroll, *Brit med J*, 1/1931, 74. Five cases of tetanus treated with doses of from 160,000 to 200,000 units of antitoxin—sodium Luminal and Avertin used as sedatives. Avertin more efficacious in producing relaxation.—E. T. Freeman, *Brit med. J.*, 1/1936, 552.

### **Tetanus Antitoxin (Veterinary).**

The horse injected with tetanus antitoxin is not rendered *permanently* immune. *Protection* is a matter of weeks or months at the outside.

Between 60° and 66° an increase in temperature of 1° increases the rate of destruction in tetanus antitoxin 1.85 times. Phenol also has a markedly destructive effect.—Gerlough and White, *J Immunol*, 11/1934, 367.

**Tetanus Anatoxin (Toxoid).** To produce immunisation and prevent the development of delayed tetanus, an anatoxin (toxin treated with formaldehyde) has been recommended, and in 1931 the use of this anatoxin was officially recommended for the prophylactic treatment of wounded soldiers in the French army. Every wounded man, in whom development of tetanus was feared, received 1.5 ml. anatoxin subcutaneously, followed some minutes later and at a different site, by a suitable dose of serum, a second dose of anatoxin being given 20 days, and a third 30 days, later, 2 ml being injected. Tests of the antitoxin titre of the blood serum of 240 patients six months after the injury showed contents varying from 1 unit to  $\frac{1}{10}$  unit per ml, indicating the existence of a definite degree of immunity.—E. Saquépée, *Paris Méd*, June, 1933, 491.

Alum-precipitated tetanus toxoid in a dose of 1 ml induces a higher degree of immunity than three doses of toxoid without alum.—D. H. Bergev, *J. infect Dis*, 1934, 55, 72.

Two injections of alum-precipitated toxoid better than three of unprecipitated toxoid.—Jones and Moss, *J Immunol*, 1/1936, 115.

Persistence of tetanus antitoxin in man, 2 years after active immunisation with toxoid.—Sneath and Kerslake, *Brit med. J*, 11/1935, 290.

### **Tuberculosis.**

*For tuberculous milk as source of infection, vide Vol. II under B. tuberculosis*

**Tuberculosis Notification Order.** This order was designed to complete the organisation for ensuring notification of all cases to health authorities. A medical practitioner is not required to notify any case which has already to his knowledge been notified either under this Order, under the Poor Law Order (1908), or under the Hospitals Order, if the notification has been made to the M.O.H. of the area within which the patient resides; but if a patient who has been notified in the area of one Sanitary Authority removes into another, a fresh notification to the M.O.H. of the new area should be given. Patients in a prison, reformatory, school or lunatic asylum and patients in a Poor Law Institution, or under the care of a Poor Law District M.O., are not to be notified under this Order, nor are applicants for life insurance, nor a passenger or member of the crew of an emigrant ship, nor an inmate of any building, ship, vessel, boat, cart, van, shed, or similar structure belonging to His Majesty the King. Multiple notification results, but steps are taken to prevent it affecting statistics on prevalence.

**Australian quarantine.** Any passenger deemed to be suffering from tuberculosis, even in an early stage, is usually prohibited from landing—or a heavy bond is exacted binding him to leave if not recovered at the end of six months.

**Progress of Infection in Phthisis.** Tuberculosis causes immunity—the resistance is specific—the apparently strong may succumb to it. There is a menacing danger of the infection of new areas; absolute rest in bed in the early stages will avoid it.

Some degree of immunity to bovine tuberculosis can be induced in calves by injecting them with cultures of the human type. Similarly in man the disease tends to confer some immunity, and it is on the acquisition of the new or improved powers of resistance, which are the cause of the immunity, slight though it may be, that the hope of recovery mainly depends. In man, as in the ox, the severity of a tuberculous infection is largely determined by the number of bacilli gaining entrance at the start. In its tendency to produce immunity tuberculosis differs from other diseases only in degree. During the course of infection the powers of resistance are constantly increasing.

A tuberculosis patient, under a doctor, will improve for a time, no matter what drugs, vaccines, or treatment be employed, owing to the nursing, regulation of food, exercise and sleep, etc. If this were recognised, "treatments" would diminish. Records must be kept for years before the value of a remedy can be gauged.—W. E. Dixon, *Brit. med. J.*, 1/1925, 813, 815.

League of Nations Report on mortality from tuberculosis in various countries during the last 50 to 80 years.—*Brit. med. J.*, 1/1931, 1127.

In Glasgow 12% of the population live in one-apartment houses and 48% in two apartments. Domiciliary treatment of advanced cases in such conditions impossible. Preventive methods employed. Death-rate there from phthisis now a quarter of what it was in 1870.—A. S. MacGregor, *Brit. med. J.*, 11/1930, 725.

About 36,000 people die from tuberculosis every year in England and Wales, though the death-rate in 1929 was 44% less than in 1918. Next to nothing is done for after-care, though money is devoted to new sanatoria.—*Brit. med. J.*, 1/1930, 836.

Printers have a high mortality from tuberculosis, though a low general death-rate.—*Lancet*, 1/1929, 679.

Fowler's suggestion to inoculate milk with live tubercle bacilli as a prophylactic against tuberculosis never thought of.—F. N. Moos, *Lancet*, 1/1930, 832.

The Indian populations of Manitoba and Saskatchewan are literally soaked in tuberculosis.—A. S. MacGregor, *Brit. med. J.*, 11/1930, 725.

Outlook on tuberculosis.—Sir R. W. Philip and others, *Brit. med. J.*, 1/1931, 239.

*For the relationship between human and other forms of tuberculosis and tests to distinguish types of B. tuberculosis, see Vol II*

## Tuberculins.

There is no consensus of opinion either as regards the proper variety of tuberculin to use or the correct dose to employ. The preparations now described are **Old Tuberculin**, **Albumose-Free Tuberculin** or **T.A.F.**, **Tuberculin T.R.**, **Bacillary Emulsion** or **B.E.**, **Beranek's Tuberculin**, **Raw's Vaccine**, **B.C.G.**, and certain other modifications.

**Tuberculinum Pristinum (B.P., U.S.P. XI).** *Syn.* TUBERCULIN KOCH (P.G. VI).

This is an amber-coloured liquid—a mature glycerin broth culture of the tubercle bacillus concentrated to  $\frac{1}{10}$  its volume, filtered, and diluted to the requisite standard with 50% v/v aqueous glycerin.

*The Therap. Subs. Regns. 1931 and the B.P. specify Old Tuberculin as proper name for this; if with the suffix "T" the tuberculin has been made from a case of human infection, while "P.T." indicates made from bovine infection.*

For details of the standard and tests for potency, etc., see Vol. II.

It has been used (a) as a *diagnostic* both in man and beast (see p. 976), and (b) for treatment, but is now little used for this purpose. Tubercle vaccine and tuberculin A.F., *q.v.*, replace it. It is, however, still used in the "dispensary" treatment of Camac Wilkinson, *q.v.*

**Effects of Injection.** The tuberculin seems to act upon the tuberculous lesions, and even partly destroys them—it is not definitely destructive to the tubercle bacilli—or their surroundings, and subsequently there is a risk of further symptoms from blood poisoning dependent on this. The tuberculin may cause a serious fall in blood pressure, leading even to a fatal issue; in other cases there have been congestion and hæmorrhage or other irritant effects have been produced.

**Contraindications** for the injection are laryngo-tuberculosis, cardiac troubles, diabetes, nephritis and pregnancy. In epilepsy and neurasthenia it should be given with the greatest caution.

The general reaction usually sets in about 8 to 16 hours after the injection—more or less severe attack of shivering, with headache and pains in the limbs.

At the point of injection, redness appears after 1 to 2 hours, and gradually an infiltration shows itself, varying in size from that of a farthing to that of half-a-crown, the absorption of which may take several days.

The height of the reaction is indicated by a profuse outbreak of sweating, a lessening of all the other symptoms and a more or less speedy return of the temperature to normal. Generally the entire reaction is over in 24 to 36 hours. There may be slight lassitude, and in the case of phthisis an increased expectoration, disappearing in a few days.

In lupus patients, besides the general reaction, a marked local reaction sets in.

**TUBERCULOUS MENINGITIS** treated with daily intrathecal injections of 1 to 3 mg of old tuberculin (T.A.) suspended in cerebrospinal fluid by lumbar puncture.—C Worster-Drought, *Med Pr.*, 1/1922, 514

**GENITO-URINARY TUBERCULOSIS** massive doses of P.T.O., P.T. and Old T. to 1.5 ml.—R. Creasy, *Lancet*, 1/1920, 542. See also *Brit med. J.*, 1/1927, 491.

**Unguentum Tuberculin (Old).** Lupus vulgaris has been diagnosed and treated by use of old tuberculin ointment—5% of old tuberculin in a basis of soft paraffin. This is well rubbed in for one to two minutes, and is also applied by means of a bandage to the affected area—the part being previously cleansed and crusts, if any, removed. On removal of the application, varying degrees of hyperæmia and swelling are seen in the actual lupus tissue, with a moderate amount of hyperæmia with reddish papules extending one or two inches into the surrounding healthy skin (Moro reaction *q.v.*). After cleaning the surface, similar applications for treatment are made for the next three or four days, till the lesion closely resembles that produced by the application of a salicylic acid plaster. This typical reaction only obtains in the actual disease and does not extend into the surrounding healthy skin. The pain produced may be considerable.

**Tuberculin Bouillon Filtrate.** *Syn.* TUBERCULIN B.F., T.O.A., TUBERCULIN-ORIGINAL ALT. A germ-free tubercle bacilli bouillon culture, resulting from filtering mature cultures;

with or without the suffix T.O.A. or P.T.O., *i.e.*, from human or bovine source.

*Dilutions greater than 1 in 10 do not keep well.*

It has been used in the "dispensary treatment," (p. 973). Asthma and hay fever have been treated with it on empirical lines.

**Vacuum Tuberculin and Vacuum Bovine Tuberculin** are analogous to T.O.A. and P.T.O. concentrated to  $\frac{1}{10}$  volume—for treatment of special cases (not for diagnosis) where a mild effect is desired. *Initial dose*—0.1 ml. of 1 in 100,000 dilution twice or thrice a week, at most doubling on second occasion. If reaction occurs, 8-day interval after complete abatement of symptoms. Diluent, normal saline with 0.5% of phenol.

### **Tuberculin A.F. (ALBUMOSE-FREE) (P.G. VI)**

*Distinguish from diphtheria toxoid-antitoxin floccules, also known as T.A.F.*

*Dose* (Initial)—0.00001 ml. in pyrexial cases, 0.0001 ml. in apyrexial cases. Subsequent doses are determined from a study of the resulting reactions—constitutional, or general and focal. As a rule, reactions should have subsided before more is given.

A light amber-coloured liquid, the product of the tubercle bacillus grown in a special culture medium free from albumoses and peptones, evaporated to  $\frac{1}{10}$  its volume and finally filtered. It may contain 0.5% of phenol and is standardised at Frankfurt-a-M.

This preparation, as already indicated, may replace old tuberculin. It is used as *diagnostic* by conjunctival, intracutaneous and percutaneous application.

*For treatment* it is employed subcutaneously where a fold of skin and underlying tissues can be raised. Reactions obtained are thought to be specific, and anaphylactic symptoms are excluded in consequence of the absence of non-specific proteins.

**Nordalin ("A" and "B").** (*Harwoods Chemists Ltd, Watford*). The "active substance" is a sulphoguaiacolic precipitate of the plasma of specially prepared animals. "A" contains 0.0025 g. of active substance with 0.00004 g. of Koch tuberculin; "B" contains 0.035 g. of active substance alone. Supplied in tablets for use in conjunction with Recytel (q.v.) in all forms of tuberculosis.

**Recytel** (*Harwoods Chemists Ltd, Watford*). Lipidogenous organic extract of the subcutaneous tissues in combination with iron, phosphoric acid, magnesium and albumoses. *Dose*—1 tablet 3 times daily. In exhaustion states generally, in asthenia and premature senility; also in tuberculosis in conjunction with Nordalin (q.v.).

The Nordalin treatment of pulmonary tuberculosis consists in giving three separate preparations by mouth and in tablet form: (a) a lipidogenous organic extract called "Recytel"; (b) the active substance "Nordalin A" to which is added Koch tuberculin; (c) the active substance without the Koch tuberculin called "Nordalin B." The Nordalin A tablet contains both human and bovine tuberculins. The treatment can be used in all stages of the disease, and in no way interferes with pneumothorax—indeed, it is likely to prove of much assistance. In most cases, patients progress right from the start, regain their appetite and energy, put on weight, and a positive sputum becomes less in quantity, finally negative, and then dries up—S. G. Tippet, *Med. Pr.*, 1935, 143.

**Catsalan** (*Swiss Serum and Vaccine Institute, Berne, Coates & Cooper, London*). Non-toxic albumose prepared from old tuberculin. For intramuscular injection in the treatment of all forms of tuberculosis, especially in the early stages.

**Tubercle Vaccine.** This is the proper name under the *Therap. Subs. Regns.* 1931 for preparations made from the bacillary

substance by growing the organism on artificial media. They are suspensions of the killed organisms or products derived from them, and are often referred to as "New Tuberculin."

**Vaccinum Tuberculinum (B P C)** *Syn.* TUBERCLE BACILLARY EMULSION, B E

The original "new tuberculin" of Koch Human type, bovine type, or the two mixed, are available

*Dose.*—0.00001 to 0.00002 ml. as a rule to begin with The dose is increased carefully at a rate which causes little or no rise in temperature ( $1^{\circ}\text{F}$ ), and with intervals of about 1 week With the small initial dose stated it is very exceptional for any reaction to appear Should a rise occur, the dose should not be exceeded until the temperature has reached its previous level.

As proof of the immunising properties of his T.R. and other preparations, Koch demonstrated the production of specific immunising bodies, which he called *agglutinins*. The difference between B E and T.R. is that B.E. contains the *entire body substance of tubercle bacilli*, whilst with T.R. the *soluble constituents* of the bacillus are first rejected The soluble endotoxins are thought to play an important part in the production of agglutinins and are contained in B E

*B.E. is, therefore, a suspension of entire pulverised tubercle bacilli in a mixture of equal parts of glycerin and water. 1 ml. contains 5 mg. of thoroughly dried tubercle bacilli*

The bacilli, grown on a solid medium, are pulverised by prolonged grinding in a ball mill. Before grinding they may be either alive or killed by heat The powdered product is emulsified in normal saline and diluted so that 1 ml. contains 5 mg. of powdered bacilli A 1% dilution of the original is sometimes called "Dilution No. 1," a 0.1% is No. 2 and so on

*Bold dosage* was advocated by the German school Starting with the same initial dose (0.00001 to 0.00002 ml.), at 1 or 2 days' interval, the dose was rapidly increased from twice to 5 times the dose at each injection, until definite reaction appeared with a rise of  $2\frac{1}{2}^{\circ}$  to  $5^{\circ}\text{F}$  in temperature. As soon as such violent reaction developed, much longer pauses, 6 to 8 days, were made The injections were increased to 4 ml. undiluted B.E. Koch regarded the immunisation as complete only when the patient could tolerate this without reaction. The larger doses of 2 to 4 ml. were only injected at intervals of 2 to 4 weeks.

In exceptional cases (*English dosage*) the initial dose may be as minute as १०००००० mg. bacillary substance with gradual rise—the limit being ३६० mg. of bacillary substance (= 0.0004 ml.). *Average doses* are respectively ३००००० mg. (= 0.00001 ml.), ३०००० mg. and ३००० mg. diluted in 1 ml.

**Tuberculin T.R. Human, Bovine and Mixed Types.**

*Dose*—Initial (subcutaneous), 0.00001 to 0.0001 ml. according as the case is pyrexial or not, rising gradually to 0.2 or even 1 ml Dilutions are made in 1 ml., using 20% glycerin as diluent.



*N.B.—Doses should be stated in decimals and by no other method.*

Although a stereotyped increase of dose is not advised, the following scheme will be useful as a guide (reading downwards in each column):—

0.00001 ml.	0 0001 ml.	0 001 ml.	0 01 ml.
0.00002 "	0.0002 "	0.002 "	0.02 "
0.00003 "	0.0003 "	0 003 "	0.03 "
0.00004 "	0 0004 "	0.004 "	0.04 "
0.00005 "	0 0005 "	0 005 "	0.05 "
0.00006 "	0.0006 "	0.006 "	0.06 "
0.00008 "	0.0008 "	0 008 "	0.08 "
			0.1 "
			0.2 "

*As a rule weekly injections are given.*

Several commercial preparations made on the lines of Koch's directions for T.R. are available.

**T.R. of Koch** contained 2 mg. of solid substance, *not* 10 mg. as originally stated. It may be recalled therefore that:—

0 00001 (1/100000) ml. of T.R. = 0.00002 (1/50000) mg. (or 0 00000002 g.) of solid substance.

**Bold dosage.**—The large doses advised by Koch, starting from 0.0002 ml. and repeated every second day with moderate increase of dose so that a rise of temperature greater than 0.9°F. was avoided, are not now generally administered.

The *English School* start with smaller initial dose (as already outlined) and do not look for any marked rises in temperature.

**Tuberculosis Immunising Vaccine (Nathan Raw).** *Syn.* TUBERCLE VACCINE "R" Raw states that virulent tubercle bacilli—after years of subculturing—can be attenuated. The present cultures (subcultured monthly) represent the 216th generation—still true to type, but even when injected in large quantities into animals they are non-tuberclogenic and avirulent.—*Brit. med. J.*, 1/1925, 741. In his opinion this remedy should be of greatest value, not only in curing the disease, but also in its prevention, by protecting the human body against attack. Cattle can be rendered immune to virulent bovine bacilli by previous inoculation with virulent human bacilli. There is a marked antagonism in the human body between human and bovine infections. These two organisms cannot flourish in the body at the same time.

Extended clinical investigation at Liverpool showed that the human body is attacked by two quite distinct forms of tubercle—the one conveyed by direct infection and attacking chiefly the lungs (so-called consumption), the other, the surgical form, conveyed by milk from tuberculous cows and developed in the first few years of life. A vaccine made from bovine cultures should be used in the treatment of human infections and *vice versa*.

**Raw's Vaccine** is a bacillary emulsion of the bacilli containing all the products of the bacillus. It is non-toxic and avirulent, and produces no reactions even in large dose.

**Dose.**—0 001, 0 002, 0 003, 0 004, 0 005 and 0 006 mg. for immunising susceptible children at weekly intervals, repeated in three months.

For treatment of the active disease, commence with 0.001 and increase to a maximum of 0.025 mg. Twelve injections should be given at intervals of seven days. Vaccine should be freshly made. Results in suitable cases excellent.—*N. Raw, Brit. med. J.*, 1/1921, 595; *Lancet*, 1/1921, 693. See also *Brit. med. J.*, 1/1925, 741, and *Lancet*, 1/1921, 1305.

Results of treating 88 cases of tuberculosis with N. Raw's vaccine during 12 months.—*N. Raw, Practitioner*, 1/1922, 229.

**TUBERCULOSIS IMMUNITY.** As a result of the treatment of over 3000 cases of tuberculosis with every preparation of tuberculin, the author is convinced

that a vaccine prepared from an attenuated and non-pathogenic culture, free from all toxins, gives by far the best results.—N. Raw, *Practitioner*, 11/1923, 317.

#### General References to Use of Tuberculin.

If tuberculin were entirely useless it would have been discarded long ago, and would not be the subject of serious discussion 42 years after its introduction. It has definite therapeutic uses—considerable in localised and surgical manifestations; strictly limited in pulmonary forms.—R. A. Young, *Brit. med. J.*, 11/1932, 1091.

Contraindicated in active, spreading, caseous disease, or with continuous remittent or intermittent fever.—R. A. Young, Sect. of Tuberculosis, B.M.A. Cent. Meeting, 1932, *Brit. med. J.*, 11/1932, 316.

Tuberculin in certain cases acts "like a charm," in others it does little or no good, and in others again does actual harm. Except in cases of asthma, much improvement with tuberculin cannot be expected in 'sub-sensitive' cases (e.g., those which react to a 1 in 10 dilution of old tuberculin).—F. E. Gunter, *Brit. med. J.*, 1/1924, 1049.

Tuberculin treatment. Focal reaction important. Dose should be regulated so that "lumps" at the site of injection do not form. One must find the tuberculous content of the patient before the disease can be attacked successfully.—R. Robertson, *Practitioner*, 1/1922, 354.

Tuberculin "offers a certain cure in 90% of early cases." Four essential points: (i) Not to be given when patient has intermittent or continuous pyrexia, (ii) Dose to be given twice a week, (iii) Persistence until large doses are reached, (iv) Temperature taken four times a day. Recommendations beginning with P.T.O 0 0005 ml. gradually increased to 1 ml. then P.T 0 005 ml. increased to 1 ml., then Old T. 0 05 ml. increased to 1 ml. After a reaction, i.e., either general (rise in temperature, nausea and perhaps vomiting), local, or focal at site of tubercular disease, no further doses should be given for one week. Then, unless the reaction is unusually severe, the same dose should be given. In a few very sensitive cases it may be necessary to begin with as little as 0 0000002 ml. T.A.F. Minimum time for first course, five months.—Rolf Creasy, Jun., *Med. Pr.*, 1/1923, 66.

The improvement occasionally following the tuberculin reaction may be seen after the shock following other substances, e.g., normal horse serum. Apart from this action tuberculin has no therapeutic value whatever. An overdose may do considerable harm, but it is safe in experienced hands, and its dangers have been much exaggerated.—L. S. T. Burrell, "Recent Advances in Pulmonary Tuberculosis" (Churchill, 1931).

Of 267 tuberculosis specialists replying to a questionnaire only 5 used tuberculin as the main form of treatment. The majority counselled against its use in all but quiescent or slightly active cases, and 63 reported harmful results.—L. Hektoen and E. E. Irons, *J. Amer. med. Ass.*, 1/1929, 869.

TUBERCULOUS ASTHMA can be ameliorated or cured by the following technique. Commence with 0 1 ml. of tuberculin liniment (see p. 978) and double weekly till 1 ml. is given. A tuberculin rash often appears in due course at the site of application, usually accompanied by amelioration of the asthma. If not, proceed to injections, commencing with T.A.F. 0 0001 ml. and increasing weekly. If reaction or an attack of asthma ensues, return to the liniment.—F. E. Gunter, *Brit. med. J.*, 1/1929, 575.

TUBERCULIN DISPENSARY TREATMENT. W. Camac Wilkinson read a paper at the B.M.A. Meeting, 1910. Only early or suspected cases are suitable for this form of—Dispensary—treatment. The treatment should be refused to all presenting evidence of mixed infection.

None but experts should give tuberculin for diagnosis or treatment, and not even the best qualified medical practitioner should use it in treatment without at least three months' training at a tuberculin dispensary. Rather than waste money trying to teach ignorant people how to prevent tuberculosis it should be spent in educating medical men to recognise and treat the disease so as to prevent it becoming infectious. Tuberculin could reveal serious tuberculosis that could not be detected in any other way. In 1927 the Ministry of Health spent £3,150,000 in dealing with consumption. St. Pancras's share was £22,000, which allowed £10 for the treatment of each patient. At this cost, by tuberculin dispensary methods, 5 to 10 times as many patients could be treated as sanatoria could treat, with better results—the patient could often go on working and providing for his family. Sanatorium treatment a curse to the taxpayer, the patient, and the sanatorium doctor. The scientific method has not had a fair

trial in any country, because it is highly technical, difficult to learn, to teach, and to practise, and its evaluation demands exacting conditions, leading men had rejected Koch's work and teaching because they have never seriously investigated it under these conditions. Wrong doses have been given in the wrong way at the wrong time, and in the wrong cases. Experiences at the tuberculin dispensary in London showed that in all patients in Stages I and II, where tubercle bacilli were found in the phlegm, 68% were alive at the end of 8 to 10 years, and 70% able to follow their ordinary occupations, the L.C.C. results in similar cases, under sanatorium treatment, were 28% alive at the end of four years. The advocacy of tuberculin, both as a diagnostic and curative agent, rests on facts that cannot be impeached.—W. Camac Wilkinson, *Brit med J*, 11/1928, 444.

From a study of his papers his usual treatment is first a course of P.T.O., then P.T. (may be repeated courses), then Tuberculin Old—or more recently Tuberculin A.F.

"The dosage (at the Portsmouth Municipal Tuberculin Dispensary) is approximately as follows—First dose of P.T.O. is from 0.00025 to 0.005 ml, increased gradually to 0.5 or 1 ml. When this has been reached without reaction (over 100°F.), P.T. (which is said to be 40 to 50 times as powerful as P.T.O.) is given, i.e., after 0.5 ml of P.T.O. the usual dose of P.T. will be 0.01 ml until 0.5 to 1 ml is taken without reaction, when a short course of Old Tuberculin with a maximum of 0.5 to 1 ml is injected."

In support of large doses of tuberculin subcutaneously.—W. Camac Wilkinson, *Brit med J*, 1/1923, 675.

For details of Municipal Tuberculin Dispensary Treatment, see 17th Edn., p. 895.

Pulmonary tuberculosis treated with tuberculin. Method of Camac Wilkinson used as above outlined. In all about 40 injections were given, lasting over a period of six months, good results obtained.—W. Stobie, *Brit med J*, 11/1922, 473.

In a criticism of C. Wilkinson's book, "The Principles of Immunity in Tuberculosis," it is asked, "If tuberculin is of such high value, why, after so many years, is it so little used, or rather, why is it feared and condemned?"—*Brit med J*, 1/1926, 1039.

**"B.C.G." (Bacille Calmette-Guérin)**, a strain of tubercle bacillus grown on glycerinated ox bile, first described by Calmette in 1909, was subcultured 230 times up to January, 1921, when vaccination experiments were started, and was then incapable of producing tubercles. Caused a general disease in calves resembling typhoid fever, clearing spontaneously after 15 to 20 days without producing slightest tubercle formation. "B.C.G." now cultivated on potato and glycerinated veal broth or Sauton's Asparagin medium, cultures must not be more than 10 days old. It is employed for the prophylactic vaccination of the newly-born against tuberculosis, and is administered in milk at body temperature in three doses. It is harmless even in new-born infants. Up to end of 1925, 1317 new-born infants treated (of which 586 had been in contact with tuberculous cases). Of this number, 10 died of tuberculosis by end of first 6 months.

Of 882 cases reported on from one to two years after vaccination there were 7 deaths from tuberculosis and 72 from other diseases, and of 87 reported on more than two years after vaccination there were no deaths from tuberculosis. The conclusion is that mortality from tuberculosis among vaccinated cases is 0.8 per 100 living, and from all cases 8.9 per 100, as compared with 26 per 100 in the same age group of children born of tuberculous parents or living in tuberculous environment.—*Lancet*, 1/1927, 936.

Vaccination against tuberculosis (Calmette Vaccine).—*Brit med J*, 1/1926, 581. See also *Lancet*, 1/1925, 1353.

Statistics show a striking difference in the tuberculosis mortality in France existing between infants who have been vaccinated by the method of Prof. Calmette and those not so vaccinated. The procedure is to give 3 doses, each

of 10 mg of a non-virulent strain of tubercle bacilli during the first 10 days of life, and the figures represent the mortality calculated on each of the first two years of life.—*Leader, Brit med J*, 1/1927, 845 See also *ibid*, 897, 1082, in which limitations in the value of the statistics are suggested by M Greenwood

Destructive criticism of B C G Figures unsatisfactory Calmette's claims "optimistic."—*Brit med J*, 1/1928, 364

Prophylactic inoculation of adults with B C G —*Lancet*, 11/1928, 931

Over 300,000 doses issued by the Pasteur Institute during the past 7 years without a single accident The oral route only should be used by the general practitioner —*Per Prescriber*, 1929, 253

3 doses given *per os* according to Calmette's prescription during the first 10 days of life, repeated at 1 year, and again at 3 years After the first 10 days it may be given subcutaneously if two negative cuti-reactions obtain at 8-day intervals Dose—0.01 mg to 0.5 mg—*ibid*, 254

Prof Calmette's statements on B C G to Roy Soc Med The untreated child is auto-vaccinated by milk, food, dust, etc In Calmette's method an attenuated strain (230 passages) of living organisms is employed Mention of first child treated (born of tuberculous mother and grandmother) 10 years after the child is healthy and well—*Brit med J*, 1/1931, 1070, 1080

In France one child out of every five is inoculated within the first week of life with B C G vaccine, the average number of vaccinations each month being 10,700 Outside France more than half a million children have been vaccinated The general mortality, including all traumatism as well as diseases, is 4.6% in the vaccinated against 25% in the non-vaccinated during the first year It is perfectly safe to revaccinate at 1, 3, 5 and 7, such children as are specially incited—*Per J Amer med Ass*, 1/1933, 130

Reasons for absence of official support for B C G vaccination in Great Britain, as submitted to the Office International d'Hygiène Publique (Paris) by Sir George Buchanan, and Professor Calmette's reply—*Lancet*, 1/1933, 653

**Duration of Immunity.** Complete immunity against tuberculous infection by the mouth can be conferred on calves by the intravenous inoculation of B C G The immunity lasts a variable time Under the conditions of experiments, the duration of absolute immunity ranged from nearly 6 months up to more than a year It may be suggested that a state of relative immunity would have existed for much longer periods, since the calves which became infected in the later stages of the experiment showed disease of less extent and greater chronicity than the controls

**Immunity after Revaccination.** Revaccination with 100 mg. B C G. restored the immunity, but the protection was complete in a smaller proportion of calves than after primary vaccination. When compared with calves receiving a single course of B C G which were tested at the same period after vaccination (6 months) the results appear to indicate that revaccination does not give as good an immunity as primary vaccination, but the numbers of calves are too small for definite conclusions on that point—*Lancet*, 1/1935, 457

It has been proved that there is a definite increase in the resistance of cattle by the use of B C G vaccine, although it varies within wide limits, and the duration of the increased resistance also varies within wide limits The oral method, if one may judge from animal experiments, is not efficient One is not justified in taking the animal experiments, even those in cattle, as a reason for universal vaccination in man—*Editorial, J Amer med Ass*, 1/1936, 133

**LUBECK DISASTER.** 50 out of 246 infants rapidly developed symptoms of acute tuberculosis, with 14 deaths—*Lancet*, 1/1930, 1137 See also *ibid*, 1244.

Prof. Deycke and Dr Altstädt were both found guilty of manslaughter by negligence in 68 cases and of injury by negligence in 131 cases, and were sentenced on Feb 6, 1932, to 2 years and 1½ years imprisonment respectively The presiding judge said that although according to some experts B C G. vaccine, under certain conditions, may become virulent, the disaster had actually been caused by an exchange of B C G. with other virulent bacilli or by contamination. The negligence in the case of Prof Deycke was that he had prepared the vaccine in a laboratory where such contamination or exchange was possible, and in the case of Dr Altstädt (Director of the Lubeck Health Dept.) in not testing the cultures before distribution and in not immediately stopping distribution as soon as he was informed that there was something wrong with them.—*Lancet*, 1/1932, 365.

**B.C.G. Vaccine (Pasteur Institute, Paris)** B.C.G.: for oral administration soon after birth, 1 cg bacilli in 2 ml B.C.G.-NR: for oral use in children over

2 years and in adults, 5 cg. bacilli in 10 ml. B.C.G.-SC: for subcutaneous injection,  $\frac{1}{8}$  cg. in 2 ml.

*The following additional (unclassified) preparations are also used:—*

**Beraneck's Tuberculin** consists of a mixture of tubercle-broth filtered free from bacilli and concentrated *in vacuo*, with an extract of the bacilli made with phosphoric acid. It is stated to contain exotoxins and endotoxins and acts like a vaccine, strengthening the bacteriolytic power of the protective cells; it also exercises a bactericidal or attenuating effect on the tubercle bacillus.

It is supplied in 6 dilutions, T.Bk<sub>1</sub> to T.Bk<sub>6</sub>, viz. 1 : 10 to 1 : 1,000,000 for use.

#### **Spahlinger's Tuberculosis Vaccine.**

Method of preparation of the vaccines disclosed by M. Henri Spahlinger as a result of financial assistance on the part of a small group of people (H.H. The Aga Khan, Lord Crewe, Lord Rosebery, Lady Seaforth and Sir Arthur Stanley). Methods of preparation of a bovine vaccine for cattle immunisation and of a harmless vaccine for human prophylaxis. The original cost of £2 a dose now reduced to about 2/-. Tubercle bacilli for making the vaccine are grown under environments of food, heat, etc., natural to the disease. They are emulsified with normal saline in the absence of oxygen, then placed in ampoules and kept in the cold and dark for a year or longer and allowed to die a natural death. They thus retain unimpaired the chemical and physical structure by reason of which they are effective vaccinating agents. This replaces customary animal passage from human beings and subsequent culture on artificial media, different from the original environment which, it is claimed, alters the character of the organism. It is held that a vaccine made on the latter lines cannot deal with the disease in an animal of the group from which it was originally taken.—*Brit. med. J.*, 1/1932, 252.

Tests carried out under the supervision of the Government in Northern Ireland. A new simplified vaccine conferred a high degree of resistance against massive intravenous injection of tubercle bacilli.—Abstract from the report, *Vet. J.*, 1935, 423.

### **Tuberculin Reactions for Diagnosis.**

#### **Subcutaneous Test.**

**The test in the human being (not usually considered safe).**

An initial dose of 0.2 ml. of a 1 in 1000 dilution of old tuberculin is injected subcutaneously. If no rise of temperature follows, give 1 ml. of a 1 in 1000 dilution at least 48 hours later. If again no rise of temperature occurs give 0.5 ml. of a 1 in 100 dilution. Finally, if necessary, 1 ml. of a 1 in 100 dilution. A rise of 2.3°F. or more occurs in tuberculous subjects some 6 or more hours after the injection of tuberculin.

While Koch's subcutaneous test is definitely inapplicable to persons with pyrexia, and is unsafe in those with lesions of the easily-activated type, the chronic, productive, inert, sputum-negative cases stand the test well, and the risk is not serious. Koch's test remains the most valuable in diagnosis; the only thing against it is its risk.—S. L. Cummins, *Brit. med. J.*, ii/1932, 1090.

#### **The test for veterinary use.**

The animal is confined to its stall for 24 hours before the injection is made, and its temperature observed. 3 to 4 ml. of a 1 in 10 dilution is injected subcutaneously in the neck. The temperature is taken 6, 9, 12, 15, 18, 24 and 36 hours after inoculation. If there is a rise of temperature of 1.4°C. or more the animal should be regarded as tuberculous. With a rise of temperature from 0.8° to 1.4°C. the diagnosis is doubtful, and the test should be repeated after 1 month. This test has been proved to be of the utmost value for the diagnosis of tubercular infection in cattle. Occasionally in animals with advanced infection the

test is negative. In these cases, however, the diagnosis can usually be arrived at by other means. In a few cases, in animals suffering from echinococcus infection, a slight positive reaction has been obtained.

*After a dose of tuberculin in cattle, a further dose during 6 months may fail to produce a rise in temperature again.*

**Tuberculin Committee's Report.** Tuberculin tests in cattle. Subcutaneous test unsatisfactory under farm conditions, and ophthalmic test only regarded as subsidiary. Complete confidence in intradermal test—*Brit. med. J.*, 1/1925, 797.

**Cutaneous Test (von Pirquet).** Cleanse the inner side of the forearm with ether and alcohol. Make two similar scratches with a sterile needle 3 inches apart (avoid drawing blood). On one scratch place a drop of 1 in 4 old tuberculin in sterile water (pure old tuberculin is sometimes used); keep the other scratch as a control. Examine at 12, 24 and 36 hours. A positive reaction occurs in from 3 to 24 hours, and is usually at its height at 36 to 48 hours. The skin becomes red and slightly raised on each side of the scratch over an area 10 mm. broad; reactions under 5 mm should be regarded as doubtful.

**Intradermal Test (Mantoux).** Intradermal injections of 0.1 ml. are made into the cleansed forearm of—

- 1 Normal saline (the same as is used for diluting the tuberculin)
- 2 1 in 10,000,000 old tuberculin in normal saline
- 3 1 in 1,000,000 " " "
- 4 1 in 100,000 " " "
- 5 1 in 10,000 " " "

A positive reaction appears in 6 to 8 hours, reaches a maximum in 24 to 48 hours, subsides in 6 to 10 days. The skin at the site of inoculation becomes infiltrated and hyperæmic; in severe reactions vesiculation occurs. (Routine tests may be made with No. 1 and 4 only.)

The usual technique is to inject 0.1 ml. of 1 in 1000 old tuberculin intradermally. Extremely valuable in children. Negative result excludes tuberculosis, strongly positive suggests active tuberculous disease with bad prognosis, and mildly positive suggests tuberculous infection amenable to open-air treatment.—W. F. Gaisford, *Lancet*, 1/1931, 521.

100-fold or less dilutions used in a volume of 0.1 ml.—*Lancet*, i/1931, 873. Mantoux test more delicate than von Pirquet's test. The latter is equivalent to 0.1 ml. of 1 in 10,000 tuberculin given intracutaneously.—D. J. Dow and W. E. Lloyd, *Brit. med. J.*, ii/1931, 186.

So far as adults in this country are concerned a positive tuberculin reaction has no diagnostic significance whatever.—S. L. Cummins, *Brit. med. J.*, i/1929, 338, 522. Criticism by W. C. Wilkinson, *ibid.*, 621.

The von Pirquet test is the simplest and easiest for infants and young children: if negative, an intradermal test with 1 in 100 dilution should be carried out; in older children repeat the test, if still negative, with 1 in 10. The Mantoux Test (1 to 10 dilution) should always be carried out with a control injection of the broth used for the preparation of tuberculin. Pirquet test only positive when there is at least 1 mm. of erythema each side of scarified area, and the minimum for a positive Mantoux is an area of erythema 10 mm. in diameter, with swelling to the touch or a well-defined erythema greater in area than this. An erythema of 5 mm. or more should be regarded as doubtful, reinspected on the fourth day and, if still doubtful, the test repeated with a stronger dilution. Instead of maintaining the controversy as to the relative values of the Pirquet and Mantoux tests they should be combined as a routine (first Pirquet, followed by Mantoux 1 in 100).—G. G. Kayne and B. Weill-Hallé, *Brit. med. J.*, ii/1934, 468.

As a test for "active clinical tuberculous disease" the cutaneous and intradermal tests are too delicate. "Positive" reactions in adults cannot be interpreted to mean "active" tuberculous disease. A markedly positive reaction has, however,

serious significance during the first year of life the value of a "negative" may be very great, especially in childhood, but it is insufficient to stop short at a von Pirquet test, even with full strength tuberculin, or at a Mantoux with 1 in 1000 tuberculin, as many persons negative to these concentrations are found positive with 1 in 100 or 1 in 10—S. L. Cummins, *Brit. med. J.*, 11/1932, 1089

**Percutaneous Test (Moro).** An ointment made of lanolin and old tuberculin in equal parts is rubbed on to the skin of the chest. A positive reaction is shown by the development of reddening and papules

**Tuberculin P.P.D. (Parke, Davis, London).**

A protein which gives the skin reaction in tuberculous subjects has been prepared by precipitation with trichloroacetic acid from a solution of heated tuberculin prepared on synthetic media—F. B. Seibert and B. Munday, *Amer. Rev. Tuberc.*, 1/1932, 724

This purified protein derivative of tuberculin is recommended for diagnosis by the intradermal test in place of old tuberculin. It is recommended that the initial dose should be 0.00002 mg. of the P.P.D., and that 0.005 mg. be given as a second dose to those who fail to react to the first dose—*Amer. Rev. Tuberc. Suppl.*, 11/1934, 708

**Tebeprotin (R. Graf, Nuremberg, C. F. Thackray, Leeds)** The protein of tubercle bacilli "purified from all traces of cultural substances" and from soluble endotoxins. Issued in ampoules of various strengths for diagnosis, treatment and prophylaxis of tuberculosis

**Tuberculin Liniment.** Tuberculin Old or P.T.O., or equal parts of both, mixed with compound camphor liniment in proportion of 1 to 5 minims to 1 drachm, used for local application, e.g., in abdominal disease or pulmonary tuberculosis. An ointment using anhydrous lanolin employed for lupus or adenitis—J. Crockett, *Brit. med. J.*, 1/1922, 679

Patients treated by 0.01 ml. of tuberculin T.A.F. diluted with a suitable quantity (e.g., 0.5 ml.) of compound camphor liniment rubbed into back of upper arm. If no reaction the dose is doubled at next sitting, and doubling continued until 0.1 ml. of tuberculin is reached, after this the dose is increased with caution to 1 ml. Interesting to note that all cases of asthma reacted to 1 in 10 or 100, not one to 1 in 500. Tuberculin used as test to sensitiveness by von Pirquet's reaction, as modified by Ellis, initially—F. E. Gunter, *Brit. med. J.*, 1/1926, 1083

**Tuberculin Ointment (for percutaneous use—Philip).** Tuberculin original (Koch) 10 to 50, eucalyptol 5, Eucerin to 100 Beraneck's tuberculin is also suggested

Percutaneous exhibition of tuberculin exerts a remarkable influence on the first buddings of tuberculosis in childhood. Continued observations, over long periods, show it is capable of effecting the nearest approach to detuberculation yet realised. Used as a diagnostic and therapeutic agent, the two-fold aspect must be kept steadily in view. The local stimulation by tuberculin at each tuberculous focus is an important step. When tuberculin is rubbed firmly into the skin of a tuberculous patient it is freely absorbed and exerts a specific curative influence. Generally, a 25% preparation is convenient. In young subjects, or where there is doubt as to the number and extent of foci involved, begin with 10%. The actual amount of tuberculin used in a straightforward case (using, say, 25% dilution), may be approximately 0.1 ml. The ointment containing this quantity is rubbed into the cleansed skin, over an area of 1 or 2 square inches, by means of a small glass rod. Repeat once weekly.—Sir Robert Philip, *Brit. med. J.*, 1/1923, 493

## Typhoid.

**Vaccinum Typho-Paratyphosum (B.P., U.S.P. XI).** *Syn.* ANTI-TYPHOID-PARATYPHOID VACCINE, T.A.B. VACCINE.

Is made from cultures of typhoid and paratyphoid A and B organisms, containing 1000 million of *B. typhosus* and 500 million each of *B. paratyphosus A* (U.S.P. XI—*Salmonella paratyphi*) and *B. paratyphosus B* (U.S.P. XI—*Salmonella schottmulleri*) in each ml. F.E. VIII specifies 1000 million *B. typhosus* with 750 million of each paratyphoid organism.

**Dose.**—For immunising, two doses are given, 0.5 and 1 ml., at

intervals of not less than 7 days; an interval of 10 days is to be preferred (Some give three doses, 0.25, 0.5 and 1 ml., and the interval between doses may be extended to 14 days) The dose is given *subcutaneously* into the tissues of the upper arm just below the insertion of the deltoid. The patient should take no alcohol whatever during the 24 hours preceding and after the injection.

For children the dose should be proportional to age. Thus a child of 7 would receive one-third of the average dose.

There is no sound reason why prophylactic antityphoid inoculation should not be given to children aged 2 years and upwards, a diluted vaccine being used—Col H M Perry and co-workers, per *Lancet*, 1/1934, 584

**Contraindications.** Alcoholics react more strongly than others. Kidney disease requires caution, and there is possibly slight risk in the case of old-standing tuberculosis.

**Effects.** Tenderness at the site of inoculation is at its worst in about 18 hours. Redness may be caused. Give free use to the arm the day after injection. Malaise begins in about 6 hours. Occasionally a rigor. There is usually headache and a slight degree of pyrexia. Occasionally temperature up to 101°F, rarely 103°F.

The immunity created by prophylactic inoculation with T.A.B. vaccine remains at a high level for at least 6 months—probably for 12 or 18 months, and should an inoculated person contract the disease, its severity is diminished and the percentage mortality lowered.

**Anti-Typhoid Vaccine** (plain) is also made

Dose—1000 million and 10 days later 2000 million.

**Vaccinum Typhosum** (*U.S.P. XI*) contains not less than 1000 million bacilli per ml

**Anti-Typhoid-Paratyphoid-Cholera Vaccine.**

Syn T.A.B.C. VACCINE

1st dose—500 million *B. typhosus*, 250 million each of *B. paratyphosus* "A" and "B" and 1000 million *Vibrio cholerae*; 2nd dose—10 days later, twice these quantities

**Castellani's Tetra-Vaccine** contains:—(No. 1) 1 ml. contains 500 million *B. typhosus*, 375 million each *B. paratyphosus* A and B, also 5000 million *Vibrio cholerae*; (No. 2) contains double quantities of No. 1 per ml

Dose.—1 ml. of No. 1, followed by 1 ml. of No. 2, after customary interval

Anti-typhoid vaccine is also used for treatment.

Dose.—50, 100, 250, 500, 1000 and 2000 millions. An initial dose of not less than 250 millions can be safely used—these to be repeated or increased under guidance of the clinical signs and symptoms. It might be of value to give a vaccine of *B. coli* and *Streptococci* to raise the immunity against these organisms before they can take an active part in the process of destruction of the tissues (as in the later stages of typhoid).



T.A.B. vaccine of undoubted value in treatment of enterica; curtails pyrexia, limits toxæmia, and prevents complications.—M. L. Treston, *Indian med. Gaz.*, 1928, 479.

Small doses of anti-typhoid vaccine should be used at first, viz., 50 million, and gradually increased. Dose reduced with pulmonary complications, and treatment suspended on occurrence of intestinal hæmorrhage, also in hyperpyrexia, syncopal attacks, and much enlargement of spleen. Cardiac complications not contraindicated except during early stage.—*Brit. med. J. Ept.*, 1/1926, 43.

**Intravenously** anti-typhoid vaccine found of value in the treatment of typhoid fever. Large initial doses must be avoided. A febrile reaction exceeding 40 °C. is inadvisable. The initial dose should be about 120 million *B. typhosus* gradually increased to 200 million if necessary. Perforation, severe hæmorrhage, severe myocardial degeneration and severe secondary infection are contraindications. Mild hæmorrhage, pneumonia, mild myocardial degeneration, meningeal symptoms and severe toxæmia are indications for use of smaller doses than usual.—K. D. Fairley, per *J. trop. Med. (Hyg.)*, 1923, 368.

Efficacy of vaccine treatment still unsettled after 30 years. Barely 4000 cases have been treated. Intramuscular injection of no value; intravenous injection of a formalised vaccine of several strains shortened duration of the disease.—*Brit. med. J. Ept.*, 1/1928, 112.

#### **Internal Administration.**

Prophylactic typhoid vaccination of 850 subjects by the mouth. 9 developed typhoid fever from 1 to 12 months after vaccination. No by-effects.—Per *J. Amer. med. Ass.*, 11/1925, 1678.

A variation of Besredka's typhoid immunisation by oral administration of a vaccine is used by the S. African Institute for Medical Research, and thousands of natives have been vaccinated by this method, which consists in giving *per os* a liquid suspension of killed *B. typhosus* and *B. paratyphosus A* and *B*, and simultaneously a pill of ox bile. No unpleasant reaction or malaise is stated to follow, and immunisation is supposed to be as efficacious as by the hypodermic method.—*Brit. med. J.*, 11/1927, 1050.

Vaccine therapy *per os* effective for typhoid. Of 4410 men treated with oral antivirul, preceded by bile, not one developed typhoid in the Rhine Army, while of 549 treated without bile 0.07% were affected. The method prevents the gradual encroachment of *B. typhosus* on cells still healthy and cuts short the period of illness.—Prof. Besredka, *Lancet*, 1/1929, 1092.

Oral immunisation against typhoid in S. Africa at least equal to subcutaneous injection—quicker effect.—E. Cluver, *Lancet*, 1/1929, 1302.

**DISSEMINATED SCLEROSIS.** Good results with a treatment of anti-typhoid vaccine, neoarsphenamine and calcium chloride. The neoarsphenamine is dissolved in calcium chloride solution (10 ml. of a 10% solution), and the vaccine also mixed with calcium chloride. Initial dose of vaccine 25 million, progressively increased. 11 injections of calcium chloride and vaccine, alternating with 11 of neoarsphenamine in calcium chloride, i.e., 22 injections in all, spread over 11 weeks. First dose neoarsphenamine 15 cg., second 30 cg., and remaining 9 each 45 cg., making a total of 4.5 g. Feeling of intense glowing heat immediately after calcium chloride injection and nauseous taste after calcium-neoarsphenamine. Of 64 patients so treated, 40 were much improved, 6 of whom became symptom-free; 16 were improved, and 8 showed no improvement. Older patients and longer duration of disease, less favourable results. Recent cases with symptoms mainly of cerebellar type specially favourable.—Sir J. Purves-Stewart, *Med. Annu.*, 1928, 420. See also *ibid.*, 1925, 393.

**Typhoid Vaccine: Potency and Virulence.** The factor present in virulent strains of *B. typhosus*, and responsible for their virulence and inagglutinability, is an antigen. This antigen is distinct from the O and H antigens of *B. typhosus*, and renders the O antigen resistant to the action of the O antibody. The symbol Vi (referring to virulence) is suggested for this antigen and the corresponding antibody. The Vi antibody is demonstrable by agglutination and absorption tests; its *in vitro* titre is comparatively low. Active and passive immunisation disclose the powerful protective action of the Vi antibody. The O antibody, which is known to exert bactericidal and opsonising effects, also neutralises the endotoxin of *B. typhosus*, whereas the Vi and H antibodies are incapable of this action. With regard to prophylactic inoculation the Vi antigen must be taken into consideration, and the importance of perfect smoothness of the cultures used for making typhoid vaccines is in no way minimised. It is evident however,

that the virulence as well as the protective action of the smooth O antigen of *B. typhosus* is not the sole factor concerned; it shares its place with the Vi antigen. It has not yet been ascertained whether the facts established in experiments with *B. typhosus* are applicable also to *B. paratyphosus A* and *B.*—A. Felix and R. M. Pitt, *Lancet*, ii/1934, 186.

Anti-typhoid Sera containing O and Vi antibodies exert two separate and distinct effects: (a) the Vi antibody confers protection against infection with highly virulent strains of *B. typhosus* by suppressing the multiplication of the organisms, (b) the O antibody appears to be chiefly responsible for effecting the neutralisation of the endotoxin of *B. typhosus*. Therapeutic trials with the serum (in Palestine) showed that the effect on the toxic symptoms was stronger and more regular than that on the fever. The serum was administered either intramuscularly or intravenously in 50-ml. doses.—A. Felix, *Lancet*, i/1935, 799. Of 8 cases treated with this new serum, 7 ceased to cause anxiety within a few days of receiving the last dose, the only failure was the case receiving a very inadequate dose, who died from a local complication.—C. J. McSweeney, *Lancet*, i/1935, 1095.

**Vaccinum Vacciniae (B.P.).** *Syn.* VACCINUM ANTIVARIOLUM, VACCINE LYMPH, VACCINUM VARIOLÆ (U.S.P. XI), VACCINO ANTIVAIOLOSO, VACCINO JENNERIANO (P. Ital. V), VACCINUM ANTIVARIOLICUM (P. Belg. IV).

The substance obtained from the vesicles produced by inoculation of vaccinia virus on the skin of healthy animals.

To meet the requirements of the Therap. Subs. Act, 1925, the animals used must be healthy, the animal after lymph collection must be examined *p.m.*, the lymph must be treated with glycerin or other partial disinfectant (*v. postea*), it must be continuously in cold storage at below 0°; each tube must contain enough for one human subject. A label on the box or carton must show the proper name, name and address of maker, number of licence, a distinctive batch number, the date of completion of manufacture after testing for organisms, and a statement that the potency cannot be relied on for more than 7 days unless it is kept at below 10°.

In emergency a larger amount may be issued in sterile containers of larger dimensions.

The seed lymph used in this country is derived from calf lymph received from Cologne in 1907, its quality being maintained by cutaneous passage through the rabbit (repeated transference from calf to calf being found to lead to deterioration).—Min. Health Com. of Vaccination, *Brit. med. J.*, ii/1928, 266.

Its potency is maintained for long periods if stored at 0°. Between 0° and 5° it may be expected to remain potent for three months, between 5° and 10° for four weeks only, and above 10° not more than seven days.

Cowpox, or rather the artificially inoculated form of the disease termed *vaccinia*, is *variola* modified by transmission through the bovine animal.

The Vaccination Order, 1929 (framed on the Report of the Rolleston Committee—*vide infra*) instructs public vaccinators to make single insertions of lymph instead of the previous 4 insertions, multiple insertions being available to those desiring them. Re-vaccination is to be encouraged at the ages of 5 to 7 and 14 to 16. In a covering letter, the importance of primary vaccination in infancy is emphasised, and as "post-vaccinal nervous disease" occurs mainly

in children of school age or adolescents who have never been vaccinated, it is not considered wise to press for vaccination of such persons (unless directly exposed to infection) while the small-pox prevalent in this country retains its mild character. The new Order came into force on Oct 1, 1929—*Lancet*, 11/1929, 399, 411.

Glycerinated calf lymph has advantages over that obtained even from healthy children (as used in the past). Attenuation by passage of the organism through an animal of greater resistance to the disease than man is known as "Jennerisation." The place of insertion should be small, otherwise the reaction is too great. The amount of protection afforded seems to be greater than that afforded by humanised lymph. Glycerinated lymph is recognised as the safest lymph for vaccination, and by the Vaccination Acts Amendment Act, 1898, it is enacted that if a child has not been vaccinated when 4 months and 1 week old, the public vaccinator of the district shall visit the home of the child, and shall offer to vaccinate the child with glycerinated calf lymph free of charge.

Chloroform water has been recommended to replace glycerin to kill off extraneous bacteria, more rapid effect. Urgent demands for vaccine, as in an epidemic, could be met by this method with a supply of vaccine in 14 days, instead of the month or 6 weeks necessary for glycerination.

A rapid process of rendering calf lymph bacteria-free—M. Coplans, *J. trop. med. (Hyg.)*, 1926, 122.

Calf vaccine, diluted 10 to 50-fold with N/50 phosphate solution (pH 7.6) or with saline or sterile water, reduces risk of post-vaccinal encephalitis, and gives more satisfactory "takes."—S. P. Bedson, *Lancet*, 11/1929, 920.

Combined use of living virus and immune serum for immunisation against virus infections. Immunisation against vaccinia and yellow fever has been obtained in monkeys by using immune serum and living virus.—J. M. Hindlay and E. Hindle, *Brit. med. J.*, 1/1931, 740. Criticism of immunisation against vaccinia.—J. Bland, *Brit. med. J.*, 1/1931, 871.

For earlier references see 20th Edn.

### **Views on Compulsory Vaccination.**

An exceedingly mild form of small-pox has been endemic in this country for several years. Ought we not seriously to consider whether a disease which causes such slight constitutional disturbance, so few deaths, and so few (if any) after-results, really calls for the elaborate and expensive system of hospitalisation maintained for it? Moreover, the results of vaccinia are not negligible, and while the number of deaths from small-pox is much over-stated, there is a possibility that those from vaccinia may be understated. Is protection against the present type of small-pox worth the price being paid for it? Our views about vaccination are changing, and would change even more quickly had it not been a part of the official creed.—J. W. Carr, *Lancet*, 11/1928, 757.

Even if the prevalent (mild) type of small-pox can be trusted to breed true, there still exists, side by side with it, the old dangerous type. We may experience a reversion to the horrors of the eighteenth century.—Prof. Greenwood, *Brit. med. J.*, 1/1930, 398.

Small-pox (variola minor), of a mild character, showed increased prevalence during 1930 in London and some parts of the provinces. The total number of cases was 11,839, with 28 deaths. Analysis of 10 years' figures suggests that in an area where the disease has succeeded in establishing itself it tends to increase to a maximum during the 4th or 5th year of incidence and then declines.—Sir George Newman's Annual Report for 1930, *Brit. med. J.*, 11/1931, 658.

Variola major has virtually disappeared and its place taken by trivial form of small-pox—variola minor—non-fatal, not permanently disfiguring and not much more serious clinically than chicken-pox. Variola minor is a distinct entity which might be regarded as breeding true, with no satisfactory evidence that it changed into variola major. During 1922-33 there were 81,080 cases of variola

minor with 254 deaths (0.3%), in the majority of which small-pox was only a secondary cause. Variola minor so trivial it was difficult to justify compulsory vaccination.—C. Killick Millard, *Brit. med. J.*, 1/1934, 302

There was no doubt that the type of small-pox now in evidence had been breeding true and could properly be called variola minor—though they might always get variola major. Legislation with regard to vaccination was certainly overdue. The powers under the Public Health Acts were not sufficiently definite.—Sir George Buchanan, *ibid.*

There would seem nowadays to be a fairly good case for the removal of the compulsory element from vaccination, providing the necessary administrative machinery is retained for possible emergencies.—S. M. Copeman, *Brit. med. J.*, 1/1934, 397

Abolition of the compulsory element and placing of vaccination on a free and voluntary basis probably favoured by the bulk of responsible opinion.—J. C. G. Ledingham, *ibid.*, 398

The case for and against the abolition of compulsory vaccination of infants.—*Lancet*, 1/1934, 1414

For further references, see 20th Edn

**Ministry of Health Committee Reports on Vaccination: Post-Vaccinal Encephalitis.** Investigations to produce lymph free from extraneous organisms, e.g., by growing the virus *in vitro* in contact with chick embryo cells, or by inoculating rabbits intracerebrally (the neuro-vaccine of Levaditi) have been carried out. Accepted methods of testing for potency—Gin's Test, Sobernheim's Test, Groth's Test, Calmette-Guérin's Test. The present method of inspecting the patient on the 7th day should be dropped and replaced by inspection during the second week, with an obligatory second inspection in the third week, also the adoption of statonal as distinguished from domiciliary vaccination. There is no evidence that vaccine increases liability to disease either generally or specifically, or aggravates disease already established. The Committee acquitted the vaccinia virus of being the sole cause of post-vaccinal encephalitis, but was unable to exonerate vaccination from playing some part, and considered that the co-operation of vaccinia with the viruses of poliomyelitis, encephalitis, or some unknown neurotropic virus, must for the present be accepted as a working hypothesis. The Committee considered that for all practical purposes the period of effective immunity after vaccination may be regarded as not less than 7 years. Owing to the prevalence in this country during the past 5 years of a very mild type of small-pox there has arisen a marked disinclination to submit to adult vaccination, the small-pox causing little discomfort, whereas vaccination means abstinence from work for manual workers. The Committee recommended the reduction of trauma to a minimum, and considered it possible to secure 100% insertion success by application of lymph to a single linear insertion  $\frac{1}{4}$  inch long.—*Brit. med. J.*, 11/1928, 266

A further report issued by the Committee in 1930 supplements Part II of the 1928 report, and consists in the main of a record of the circumstances of 90 cases of post-vaccinal nervous diseases subsequently brought to notice, and in respect of the 25 fatal authenticated cases it correlates the available clinical information with the post-mortem findings. The report concludes with the statement that "although no particular lymph can be incriminated it is clearly the vaccinia virus, whatever its past history and in whatever medium incorporated, which initiates the nervous disturbance, but why this disturbance should be almost limited to a few individuals only of a particular age group is not known. The grouping of cases in place and time and the tendency to familial incidence are very striking features of the epidemiology and point, in our opinion, very strongly to the existence of some local individual predisposition in the widest sense of that term"—*Brit. med. J.*, 1/1931, 64

#### League of Nations Commission Report.

The report quotes extensively from the first Rolleston Committee's report (see above). The fact is emphasised that the term post-vaccinal does not necessarily imply propter-vaccinal, as coincidental disease of the brain and nervous system must be allowed for in the millions treated with vaccinia yearly. Encephalitis also occurs as a complication of numerous infections, e.g., measles and toxæmia. The Commission, however, considers that there are practical reasons for viewing post-vaccinal encephalitis as a *separate* pathological and clinical entity. The risk may be exaggerated. From 1923 to 1927 only 139 cases were reported in Holland (41 fatal), yet this has been sufficient to cause temporary suspension of

vaccination laws relating to children. In England and Wales 62 cases, with 36 deaths, occurred from November 1922 to November 1923, and 25 cases, with 12 deaths, between January 26 and September 27, the bulk occurring in children from 3 to 13. The Commission concludes that the virus of vaccinia itself is not responsible, but rather some unknown factor—a filter-passing or latent virus.

Only the treatment to which the lymph seed is subjected determines the quality of the lymph, the origin of the strain used being of no significance. While the passing of the vaccine through rabbits is unobjectionable, neurolapine obtained by intracerebral injections in rabbits, and testicular-lapine, differ from ordinary vaccine. The medical officers of vaccine institutes should themselves undertake human vaccination to study the potency of the lymph they make, the bare report "successful" or "unsuccessful" being of no value when the vaccine reaction is not described in detail. In primary vaccination the proportion of insertion successes should be noted, and in re-vaccination the reaction should be described as one of three classes: (1) Reaction of primary vaccine type (Jenner's pustule), (2) accelerated reaction (vesicular reaction) "modified vaccine," (3) allergic or early reaction (papular reaction).

The technique and methods used in different countries should be carefully defined and recorded, and judged in respect of immunity afforded, so that a satisfactory technique for universal adoption may be evolved.—*Ser. L o.N.P.*, 1928, iii, 12.

A review of the advances in the study of vaccination since 1930—O. K. Wright, *Lancet*, i/1933, 823.

**POST-VACCINAL ENCEPHALITIS.** A fatal case after primary vaccination of a boy *æet* 14, with Government lymph, 4 insertions, 3 of which "took well." Patient died 16 days after vaccination, duration of illness being 6 days.—G. N. Grose, *Lancet*, ii/1929, 381, *cf. ibid.*, i/1929, 221, and *Brit. med. J.*, ii/1929, 324.

Encephalitis (with possibly very rare exceptions) follows primary vaccinations only. It does not occur after unsuccessful vaccination. There is no evidence that it is due to a secondary infection. *It is independent of the method or animal used in preparing the lymph.* Very young children seem to escape it.—J. F. Taylor, *Lancet*, i/1929, 1302, Leader, *ibid.*, 1310.

Acute disseminated encephalomyelitis following vaccination.—C. D. Coyle and E. W. Hurst, *Lancet*, ii/1929, 1246.

Post-vaccinal encephalitis in Germany and Sweden. In Germany very rare after re-vaccination, and relatively uncommon when primary vaccination is performed under the age of 1 year.—*Lancet*, i/1930, 525.

Lesions of disseminated encephalomyelitis following small-pox indistinguishable from those of the disease following vaccination, measles, etc.—A. G. Troup and E. Weston Hurst, *Lancet*, i/1930, 566.

Small-pox and vaccination in light of modern knowledge. Post-vaccinal encephalitis considered.—J. McIntosh, *Lancet*, i/1930, 618.

Zoster, varicella and encephalitis. Lumleian Lecture on.—W. Russell Brain, *Brit. med. J.*, i/1931, 81, 104.

A review of recent data. Netherlands, England, outside Europe, Continent. Pathology.—*Lancet*, i/1931, 97.

Post-vaccinal encephalitis is *not* an extremely rare disease. About 1000 cases thought to have been recorded.—J. C. G. Ledingham, *Brit. med. J.*, i/1934, 398.

5 cases were reported in 1934, with 4 deaths, the ages varying from 6 to 20.—*Rep. med. Offr Minst. Hlth, Lond.*, 1934, 19. None in 1935—*ibid.*, 1935, 39.

### Whooping Cough (Pertussis).

**Vaccinum Pertussis (B.P.C.).** *Syn.* PERTUSSIS VACCINE, WHOOPING COUGH VACCINE, BORDET-GENGOU BACILLUS VACCINE.

A sterile suspension of *B. pertussis* (*Hæmophilus pertussis*). For details of the bacillus, see Vol. II.

Is of service in lessening the violence of the paroxysms and shortening the duration of the attack.

As *B. influenza* (Pfeiffer) and the pneumococcus commonly accompany Bordet's bacillus in whooping cough, the incorporation of these two organisms in vaccines used for *treatment* is likely to be beneficial. For *prophylaxis* either a vaccine prepared from

Bordet's bacillus alone or the mixed vaccine containing also pneumococcus and Pfeiffer's bacillus may be used.

Of 100 cases of whooping cough in children from 0 to 12 years treated with Bordet-Gengou vaccine good results were obtained in all but 4. Three injections intramuscularly of 3,000 million bacilli usually sufficient.—*Brit. med. J. Epit*, 1/1926, 56.

A review of the literature during recent years shows that much more satisfactory results are obtained with larger doses than those formerly recommended.

**Dose.**—For *prophylaxis*, in non-epidemic periods, children may be given three doses each of 2000 millions Bordet's bacillus at weekly intervals. Contacts should have similar doses at intervals of 2 or 3 days. Adults—twice above doses. For *treatment*, children 400 millions, increased to 2000 millions at intervals of 24 or 48 hours. Adults—800 millions increased to 4000 millions.

With these doses may be included appropriate amounts of *B. influenzae* (Pfeiffer) and pneumococcus. These vaccines do not produce much reaction even in young infants.

The nature of the culture medium used for the preparation of the vaccine is of great importance in regard to antigenic capacity. Freshly-isolated strains should be grown on media containing fresh blood in order to retain the pathogenic phase I, *see* Vol. II, 20th Edn., p. 627.

There is no danger in vaccines for whooping cough, and after a reasonable initial dose enormous doses can be given with safety. To get results it is necessary to give at least 5 times the ordinary amount.—At 1 year a suggested second dose is 400 millions of ordinary, or 8000 millions of detoxicated vaccine, with maximum quantities of 1000 and 25,000 millions respectively. No case treated without definite benefit since using these large amounts.—R. W. Cockshut, *Brit. med. J.*, ii/1933, 819.

Controlled experiments with vaccine in the treatment of 60 children showed that the injection in the paroxysmal stage of large doses of a pertussis vaccine prepared in accordance with modern methods and beliefs neither curtails the duration of the disease nor ameliorates the symptoms.—N. D. Begg, *Lancet*, 1/1936, 83.

**Convalescent Serum** from whooping-cough cases has been used with benefit in prophylaxis, but with doubtful benefit in treatment of pertussis. With Sauer's vaccine, immunity is completed in 4 months and lasts for years.—D. Patterson, R. H. Bailey, R. G. Waller, *Lancet*, ii/1935, 361.

**Sauer's Vaccine.** Prepared from 5-7 hæmolytic strains of the Bordet-Gengou bacillus, the culture medium containing 10% of defibrinated human blood. It contains 10,000 million bacilli per ml. **Dose**—Children under 3, 8 ml. in divided doses, 1 ml., 1 5 ml., and 1 5 ml. under the skin of each arm, at weekly intervals. Children over 3, 1 ml., 2 ml., and 2 ml. respectively.—L. W. Sauer, 2nd Congress for Microbiology, London, 1936.

**Neo-Dimetys** (*Pharmaceutical Specialities (May & Baker) Ltd., London*). Fluorised vaccine for the prophylaxis and treatment of pertussis. 1 ml. contains 500 millions of the Bordet-Gengou bacillus.

## BLOOD TRANSFUSION

This operation enables oxygen carriers and blood volume to be replaced rapidly, and is the best substitute for lost blood. Used after hæmorrhage and in shock, in anæmia when hæmoglobin is below 30%; in pre- and post-operative conditions—gastric and duodenal ulcer; in hæmorrhagic diseases, septicæmia, pneumococcal peritonitis, etc. There is, however, an incompatibility of

bloods of certain individuals, and two such incompatibles cannot act as donor and recipient respectively, since incompatible bloods are liable to agglutinate or clump and to hæmolyse each other, causing serious symptoms and even death

Individuals can be divided into four groups according to the liability of their corpuscles to agglutinate. In practice the serum of the donor can be ignored since it is so diluted by the recipient's blood, but the effect of the recipient's serum upon the donor's corpuscles must be considered

**Landsteiner's Law of Iso-agglutinins.** There are present in human blood corpuscles two agglutinable substances, A and B, which react with specific agglutinins (a) and (b) in serum. If any blood contains an agglutinable substance, it will contain the agglutinin which reacts with the alternative agglutinable substance. Thus blood which contains the A substance will contain (b) agglutinin and *vice versa*. The law is "In any blood there are always present agglutinins against the agglutinable substances absent from the same blood."

Three systems of classification of the four groups have been suggested, that devised by Moss is perhaps the most commonly used. The differences in these classifications are indicated in the following table

Moss	Von Dungern and Hirschfeld	Jansky
1	AB	4
2.	A	2
3	B	3
4	O	1

With samples of serum from the Moss Groups II and III it is possible to test the blood of any donor before transfusion. The blood of Group I does not cause agglutination of the cells of either of the other groups. Hence these individuals are "universal recipients" because they can receive blood from each of the other three groups, they cannot, however, give blood to any but their own group. Since the corpuscles of Group IV are not agglutinated by the serum of any other group, the members are "*universal donors*" and a Group IV blood is generally chosen for transfusion (See, however, S. C. Dyke, *Lancet*, 11/1927, 910). Lists of "universal donors" are kept by many hospitals.

Albuminuria, cardiac debility and marked obesity would exclude the donor — E. F. Skinner, *Brit med J*, 1/1923, 750. See also 11/1925, 516.

**Directions for Testing.** Into a "Wassermann" tube is placed a little N/10 sodium citrate in normal saline and 4 or 5 large drops of blood from the finger are added. On to one end of a micro slide is placed a drop of Group II serum, and on the other a drop of Group III serum, to each of which is added a little of the corpuscle emulsion, each mixture being stirred with a glass rod and the slide gently rocked. Agglutination is visible to the naked eye, and appears as a deposit, the particles of which may get larger until in some cases a few crimson dots float in clear serum.

Result observed	Group to which blood belongs
Agglutination with both sera	1
No agglutination with either serum	4
Agglutination with Group III serum only	2
Agglutination with Group II serum only	3

**ALTERNATIVE PROCEDURE** Some blood is taken from the recipient and centrifuged to separate the clot. A few drops of the donor's blood are taken into a 1.5% solution of sodium citrate and shaken up. A drop of the serum is mixed with a drop of the corpuscular emulsion on a slide and a cover glass placed on it. If no agglutination in 5 minutes the donor's blood is suitable. No need to determine the group.—S. Wyard, *Clin J.*, May 2, 1913, 206

### **Blood Transfusion Technique.**

Donor lies on couch with arm at right-angle and forearm supported on table. A stool with a bowl of water at 110°F. is placed beneath the elbow, and a Keynes's flask containing 150 ml 2% sodium citrate placed in the top of the flask reaching to within an inch of back of elbow. Adjust sphygmomanometer to donor's arm and raise pressure to 80 mm. of mercury. Clean front of elbow with ether and inject a drop of 1% procaine hydrochloride over selected vein. Draw off blood with a French's needle with 6 inches of rubber tubing attached; run citrate solution through needle and tube before use. Introduce needle into vein with point directed towards the hand and run blood directly into flask. The donor opens and closes his hand meanwhile, and an assistant rotates the flask.

The most suitable vein for introduction of blood is the internal saphenous, just in front of the internal malleolus. Through a horizontal  $\frac{1}{8}$ -inch incision insert cannula into vein and tie in position, running in blood by gravity through a funnel with rubber tubing attached.—A. M. A. Moore, *Brit med J.*, 11/1932, 146.

Kimpton-Brown method—a small amount of 3.8% sodium citrate used in the tube before puncturing the vein.—W. B. Gabriel, *Lancet*, 1/1928, 1255.

1 g of sodium citrate in 60 ml water for each 450 ml blood. An interesting paper with diagrams.—G. Keynes, *Practitioner*, 11/1931, 422.

A method of transfusion in which venesection is required neither on patient nor donor. The blood is delivered from inverted Dewar flask (prevents chilling of blood) through a Luer-Kaufmann syringe and venipuncture needle.—F. T. Grey, *Lancet*, 11/1932, 127.

Colebrook and Støren's method (*Lancet*, 11/1924, 1394), using defibrinated blood, gives better results than Keynes's apparatus and the gravity method.—R. Vaughan Facy, *Brit med J.*, 11/1932, 532.

A new method, employing an artificial "heart." The "heart" connects two tubes with each other. Each is fitted with a hollow needle, one for the donor's vein and the other for the recipient's. The tubing is of gum-elastic, the walls of which are coated with paraffin, preventing clotting of the blood during its brief circulation through the "heart," which beats at the rate of 60 a minute. Although there are no valves, it is impossible for the circulation to be reversed or for bubbles of air to enter it. The machinery is worked by a small 1/50 h.p. engine with a device for regulating the rate and for indicating the amount of blood transfused at any moment.—V. Pauchet and A. Bécant, per *Brit med J.*, 11/1933, 930.

### **Continuous Drip Blood Transfusion.**

The average in 87 cases was 5 pints and 29 hours, the largest figures being 11 pints and 62 hours. Present conceptions in regard



to dose needed revision; a pint was woefully inadequate for an anæmic patient, especially if he were bleeding. The principle should be made one of quantitative measurement and the restoration of a normal hæmoglobin percentage. Hæmoglobin estimations should check the infusion. The best rate was to try to increase the patient's hæmoglobin by 10% every 4 hours, *i.e.*, in the non-bleeding patient, a pint in 4 hours, or 40 drops a minute. In bleeding patients, the rate must be governed by hæmoglobin estimations. If the patients were weak there should be three stages at intervals of a few days. The method had proved extraordinarily effective. In peptic ulcer the blood could be run in as it was lost; 18 out of 22 serious cases had lived and at least half of them could not have lived without the massive transfusion.—H. L. Marriott and A. Kekwick, *Lancet*, i/1936, 86; *see also Lancet*, i/1935, 977, and ii/1935, 78, for description of apparatus.

**MALIGNANCY AND BLOOD GROUPING.** All four groups liable to malignant disease, but Groups I and II peculiarly susceptible.—*Med. Pr.*, ii/1922, 301

**MEDICO-LEGAL SIGNIFICANCE OF GROUPS.** It is impossible to identify the father of a child, but it can be stated with certainty that the alleged father is not the father in fact.—*Lancet*, ii/1928, 711.

Whole blood largely replaced by citrated or defibrinated blood—the latter leaves the leucocytes undamaged and easiest to apply. Immuno-transfusion beneficial in some desperate cases. Procedures (1) introduction of nuclei into the donor, (2) injection into donor of hypertonic saline, increasing bactericidal power.—Prof. A. Fleming, B M A. Discussion, *Brit. med. J.*, ii/1931, 802.

Blood transfusion in private practice.—J. H. Macnab, *Brit. med. J.*, i/1936, 71.

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## POISONS

For the purpose of the *Pharmacy and Poisons Act, 1933*, and of the *Poisons Rules, 1935*, a poison is any substance described in the *Poisons List*. The List is divided into two parts. Poisons included in the first part may be sold or supplied to the general public only by pharmacists; those in the second part by pharmacists and by persons whose names have been entered in a list by their local authority as defined by the Act. In either case the sale or supply may take place only from recognised premises and subject to the fulfilment of the conditions laid down in the Act and Rules.

Appended to the Poisons Rules are twelve Schedules. Those of most general interest are *Schedules 1 and 4*. The former describes those poisons in respect to the sale, supply and storage of which more stringent conditions must be satisfied than are required for the other poisons in the Poisons List. The latter describes those poisons which may be sold to the public only upon the prescription of a doctor, dentist or veterinary surgeon. In *Schedule 3* are described articles which are exempted from the provisions of the Act and Rules. *Schedule 5* indicates the only form in which certain poisons named in Part II of the Poisons List may be sold by persons whose names have been entered in

the local authority's list. *Schedule 7* describes those poisons the sale or supply of which, not being treated as a dispensed medicine (see page 994), are, in the circumstances, mentioned in the schedule, to be labelled with an indication of character other than the word "POISON." *Schedule 8* names those poisons which, except as medicines, may be transported only if certain conditions are fulfilled. The remaining schedules indicate those poisons which are exempted from the normal labelling provisions when sold or supplied in certain circumstances (*Schedule 2*); the manner in which the proportion of certain poisons may be calculated (*Schedule 6*); the form of application to be used by a person desiring his name to be entered in the local authority's list for the purpose of selling poisons in Part II of the Poisons List (*Schedule 9*); the form in which the local authority's list is to be maintained (*Schedule 10*); the form of the certificate for the purchase of a First Schedule poison to be used by a person not known to the seller (*Schedule 11*) and the form of entry to be made in the Poisons Book when a First Schedule poison is sold (*Schedule 12*).

The Poisons List is set out in full on pages 1005 to 1007; the Schedules to the Poisons Rules on pages 1007 to 1018.

Throughout these notes no reference is made to poisons which are subject to the Dangerous Drugs Acts and Regulations, and in any transaction in respect of a "dangerous drug" the requirements of the Dangerous Drugs Acts and Regulations must be complied with in addition to the requirements summarised below. The words "doctor," "dentist," "veterinary surgeon," "pharmacist" and "wholesaler" mean, respectively, duly qualified medical practitioner (i.e., registered in Great Britain under the Medical Acts); registered dentist; registered veterinary surgeon; registered chemist and druggist or pharmaceutical chemist; and a person, firm or body corporate who sells an article otherwise than to the general public. Where reference is made to poisons in the First Schedule only, such references do not apply to machine-spread plasters, surgical dressings, articles containing barium carbonate and prepared for the destruction of rats and mice, and corn paints in which the only poison is a poison included in the Poisons List under the heading of "Cannabis."

### **General Prohibitions.**

(a) In no circumstances may a poison be sold or supplied by means of an *automatic machine*.

(b) *Strychnine*, otherwise than as an ingredient of a medicine, may not be sold or supplied except to (i) persons who require it to sell again; (ii) purchasers outside the United Kingdom to whom it is to be exported; (iii) persons requiring it for dispensing, and if a doctor or veterinary surgeon, also for administration by himself or under his supervision, and (iv) persons concerned with scientific education, research or chemical analysis, and requiring it for that purpose.

## HOW TO OBTAIN POISONS FOR USE IN "BUSINESS OR PROFESSION"

A person "carrying on a business in which poisons are regularly sold or used in the manufacture of other articles" may purchase poisons from a manufacturer or wholesaler without formality. The seller, nevertheless, is required to satisfy himself that the purchaser of a First Schedule poison requires it for the purpose of his business or profession. Any other person (including organisations, hospitals or nursing homes) requiring poisons for use in his business or profession may purchase them from a wholesaler or a retailer. It will be observed that purchases may be made not only by those persons whose business or profession is directly concerned with medication, but also by others such as analysts, science teachers, research workers, and by persons such as farmers or market gardeners who use the poison in connection with agriculture or horticulture. If the poison is included in the First Schedule to the Poisons Rules, the purchaser must attend at the premises of the seller and sign the Poisons Book and supply the information necessary to enable the seller to make the required entries in that book (*see* page 995).

Alternatively, the purchaser may order the poison from the seller by post or otherwise, provided that if the poison is included in the First Schedule the order must be in writing, signed by the purchaser, state his name and address, his business or profession, the name and quantity of the article to be purchased, and the purpose for which it is required. It is not necessary to state business or profession when the purchaser is a hospital, infirmary, dispensary or clinic.

Before supplying a First Schedule poison stated to be required for the purpose of the purchaser's business or profession, the seller must satisfy himself (*a*) that the poison is used in the business or profession of the purchaser, (*b*) that the purchaser is engaged in the business or profession stated, and (*c*) if the order is in writing, that the signature of the purchaser is genuine.

### ***Emergency.***

In an emergency, a person who represents that he urgently requires a First Schedule poison for the purpose of his business or profession may be supplied if the seller is satisfied as to the emergency, and the purchaser at the time undertakes within 24 hours to attend personally and sign the entry of supply in the Poisons Book kept by the supplier or to furnish a written order as above. Failure on the part of the purchaser to fulfil such an undertaking is an offence.

## THE SALE OR SUPPLY OF POISONS

### **A. The doctor, dentist or veterinary surgeon.**

Doctors, dentists and veterinary surgeons may not sell or supply poisons except as medicines for patients under their care

If the supply is otherwise than by administration by the doctor, etc., personally, a record must be made in a book showing the date of supply, the ingredients and quantity of the medicine and the name of the patient. No record is necessary of the supply by a doctor (but not a dentist or veterinary surgeon) if the poison is not in the First Schedule, or if the medicine is supplied on a National Health Insurance prescription or on a prescription issued in connection with the health scheme of a local authority. Records where required must be made on the day on which the medicine is supplied or, if that is not reasonably practicable, on the following day. The container in which the medicine is supplied must be impervious to the poison and strong enough to prevent leakage from the ordinary risk of handling. The medicine must be distinctly labelled with the name and address of the practitioner, and if it is a liquid for external application, with the words "For external use only," together with the name of the article, *e g*, "The Liniment," "The Lotion," "The Embrocation."

It is appropriate here to mention that a prescription given to his patient by a doctor, etc., for a medicine which is a poison in the Fourth Schedule to the Rules to be dispensed by a pharmacist otherwise than at a hospital must include the following particulars —

- (i) the name and address of the person to whom the medicine is to be supplied, or in the case of a prescription of a veterinary surgeon, the name and address of the person to whom the medicine is to be delivered,
- (ii) the date,
- (iii) the total amount of medicine to be supplied and the dose to be taken,
- (iv) the usual signature of the prescriber (not his initials),
- (v) the address of the prescriber (except in the case of National Health Insurance or Local Authority prescriptions),
- (vi) if to be repeated indefinitely or for a limited number of times, bear a statement to that effect,
- (vii) if the prescriber is a dentist, bear the words "For dental treatment only," and if a veterinary surgeon the words "For animal treatment only."

Doctors and others should note that unless the prescription contains the particulars indicated above, the pharmacist is not permitted to supply the medicine. Further, unless otherwise directed on the prescription he may not supply the medicine on more than one occasion. The pharmacist **must** also retain the prescription when it is no longer valid for **further** supply.

**SPECIMEN FORM OF PRESCRIPTION FOR FOURTH SCHEDULE  
POISONS.****1. Doctor.**

<p style="text-align: center;">[Name and address of patient]</p>  <p style="text-align: center;">[Name and quantity of ingre- dients, including dose and total amount of finished product to be supplied]</p>  <p style="text-align: center;">[To be repeated X times.]†</p>  <div style="display: flex; justify-content: space-between;"><span>[Date.]</span><span>[Signature (not initials) of prescriber.]</span></div>	<p>[Address of prescriber.]*</p>
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**2. Dentist.**

As above, but in addition the words "For dental treatment only" must be written on the prescription.

**3. Veterinary Surgeon.**

As for a doctor's prescription except that "the name and address of the person to whom the medicine is to be delivered" must be inserted in place of "the name and address of patient," and the words "For animal treatment only" must be written on the prescription.

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\*Address of doctor is not necessary in the case of National Health Insurance and Local Authority prescriptions.

†If not to be repeated, this entry should be omitted. If to be repeated indefinitely the statement should make it clear that such is the intention of the prescriber. If to be repeated on a limited number of occasions, the number should be clearly stated. If desired, the prescriber may state the actual dates upon which the medicine may be repeated; he may also indicate what period of time should elapse before repeating on any occasion.

### **B. The pharmacist.**

Poisons may be sold or supplied to the general public by the pharmacist only from premises registered under Part I of the Pharmacy and Poisons Act, 1933, and only if he or his employer is an "authorised seller of poisons" within the meaning of that Act and the conditions set out below are fulfilled.

#### ***1. Dispensing medicines on prescription of doctor, dentist or veterinary surgeon.***

##### ***(A) Schedule 4 Poisons.***

The prescription must contain the particulars set out on page 992

The medicine must not be supplied more than once unless the prescriber has directed otherwise, in which case it may be supplied only in accordance with the directions. For example, if a prescription is marked by the prescriber "To be repeated X times" it may not be repeated more than X times; if "To be repeated" it may be repeated indefinitely.

The pharmacist must

- (i) mark on the prescription, above the signature of the prescriber, the date on which it was dispensed and the name and address of the seller;
- (ii) when the prescription is no longer valid to be dispensed again, retain it for two years;
- (iii) enter in the prescription book on the day the prescription is dispensed, or on the following day, the following particulars.—

- (a) the date of supply,
- (b) the name and address of the person to whom the medicine is supplied,
- (c) the ingredients and quantity of the medicine,
- (d) the name or initials and, if known, the address of the prescriber,
- (e) the date on which the prescription was given.

When the medicine is repeated, the entry in the prescription book must show the quantity of medicine supplied and a reference to the original entry.

N.H.I. prescriptions need not be copied, but should be forwarded in the ordinary way for pricing.

Local Authority prescriptions must be copied unless, in addition to the prescription, a carbon copy is supplied to the pharmacist and retained by him;

- (iv) place the medicine in a container which is impervious to the poison and strong enough to prevent leakage from the ordinary risk of handling, and transport. It will be noted that there is no obligation upon the pharmacist to put any 'dispensed' medicine in a 'poison' bottle (fluted vertically with ribs or grooves). This does not prevent him doing so, however, if he considers such course desirable.

- (v) label with the name of the seller and the address of the premises on which the medicine is sold, and if the medicine is a liquid for external application, with the words "For external use only" and the name of the article, *e.g.*, Embrocation, Liniment, etc

**(B) Poisons not included in the Fourth Schedule.**

The requirements set out under (iii), (iv) and (v) for Schedule 4 poisons (page 993) must be fulfilled, except that if the prescription is given by a doctor (but not a dentist or veterinary surgeon), and is not a First Schedule poison, no entry need be made in the prescription book.

**II. Dispensing medicine "counter prescribed" by pharmacist or to purchaser's own formula.**

**(A) Schedule 4 Poisons.**

In no circumstances may Fourth Schedule poisons be sold or supplied to the general public as a "counter prescribed" medicine or to the purchaser's own formula. A prescription from a doctor, dentist or veterinary surgeon is essential (*see* page 992).

**(B) Poisons not included in the Fourth Schedule.**

The pharmacist must

- (i) enter in the prescription book on the day the prescription is dispensed, or on the following day, the following particulars —
  - (a) the date of supply,
  - (b) the name of the person to whom the medicine is supplied,
  - (c) the ingredients and quantity of the medicine. If the medicine is repeated, it is sufficient when repeating the entry in the prescription book to state the quantity of the medicine supplied and a reference to the original entry,
- (ii) place the medicine in a container which is impervious to the poison and strong enough to prevent leakage from the ordinary risk of handling, and transport. It will be noted that there is no obligation upon the pharmacist to put any 'dispensed' medicine in a 'poison' bottle (fluted vertically with ribs or grooves). This does not prevent him doing so, however, if he considers such course desirable.
- (iii) label with the name of the seller and the address of the premises on which the medicine is sold, and if the poison is a liquid for external application, with the words "For external use only" and the name of the article, *e.g.*, Embrocation, Liniment, etc

**III. Sales "over the counter."**

**(A) Schedule 4 Poisons.**

In no circumstances may Fourth Schedule poisons be sold to the general public "over the counter." A prescription

from a doctor, dentist or veterinary surgeon is essential (see page 992).

*(B) Poisons included in the First Schedule but not in the Fourth Schedule.*

The pharmacist must

- (i) know the purchaser to be a person to whom the poison may properly be sold, or receive from the purchaser a certificate in the form prescribed in the Eleventh Schedule (see page 1017) given by either
  - (a) a householder known to the pharmacist as a responsible person of good character, or
  - (b) a householder, and endorsed by a police officer in charge of a police station

The certificate must be retained by the pharmacist;

- (ii) enter in the Poisons Book (which must be kept for at least two years after the date of the last entry) the following particulars —
  - (a) the date of the sale,
  - (b) the name, address and business, trade or occupation of the purchaser,
  - (c) the name and quantity of the poison,
  - (d) the purpose for which the poison is stated to be required;
  - (e) if a certificate is supplied by the purchaser, the name and address of the person giving the certificate and the date on which the certificate was given;
- (iii) require the purchaser to sign the entry. Where the purchaser requires the poison for the purpose of his business or profession (see page 990), it is not necessary for the purchaser to sign the entry if he supplies an order in writing giving the particulars set out on page 990, in which case the pharmacist must enter the words "signed order" in the space provided for the purchaser's signature and a reference number to identify the order. This number must also be placed on the order by the pharmacist. The order must be kept for two years. If the poison is sent by post to a person purchasing it for the purpose of his business or profession it must be sent by registered post,
- (iv) label the poison with the particulars set out below. These must appear clearly and be in a conspicuous position on the actual container of the substance and on each covering, if any, of the container except transparent covering, or covering used solely for the purpose of transport or delivery. Where the poison is contained in an ampoule, cachet or similar article, it is not necessary to label the article itself if every covering in which the article is enclosed is duly labelled.



- (a) the name of the seller and the address of the premises on which the poison is sold;
- (b) the name of the poison. If the poison is an ingredient of a *B.P.* or *B.P.C.* preparation the official name, synonym or abbreviated name of the preparation may be used, followed by the letters *B.P.* or *B.P.C.* as the case may be. If the issue of the *B.P.* or *B.P.C.* intended is not the current issue, the year of issue should be stated. Otherwise the name used must be the term used in the Poisons List, except that if that term describes a group of poisons and the poison sold is the subject of a monograph in the *B.P.* or *B.P.C.* the name, synonym or abbreviated name at the head of the monograph must be used. If the poison sold is not the subject of such monograph the accepted scientific name or name descriptive of the true nature or origin of the poison must be used;
- (c) the proportion of poison present if mixed with other ingredients in a preparation. This is not necessary if the preparation is described in the *B.P.* or *B.P.C.* If the statement of proportion is given as a percentage it must also state whether the percentage is weight in weight  $w/w$ , weight in volume  $w/v$ , or volume in volume  $v/v$ . For tablets, pills, cachets, capsules, lozenges, and similar articles, or ampoules, the quantity of poison in each and the number of articles may be stated. If the poison is contained in a *B.P.* or *B.P.C.* preparation which is an ingredient of the article sold, the proportion of the preparation to the total product may be stated;
- (d) the word "Poison," or if the poison is allyliso-propylacetylurea (*e.g.*, the proprietary article "Sedormid") or phenylethylhydantoin (*e.g.*, the proprietary article "Nirvanol"), and is made up ready for the internal treatment of human ailments, the words "Caution. It is dangerous to take this preparation except under medical supervision." The required word or words must (i) be in red or on a red background, (ii) appear either on a separate label or within a line containing no words other than the particulars with which the substance is required to be labelled by the Act or Rules, and (iii) not be modified in meaning by other words or marks;
- (e) the words "For external use only" and the name of the substance (*e.g.*, The Embrocation,

The Liniment, The Lotion, etc.) in the case of liquid medicines for external application. Mouth-washes, eye-drops, eye-lotions, ear-drops, douches and similar preparations are *not* regarded as medicines for external application for the purpose of this provision;

- (f) the words "Not to be taken" in the case of a liquid other than a medicine contained in a bottle of a capacity of 120 fluid ounces or less;
- (g) If the poison is compressed hydrocyanic acid, the container must be labelled with the words "Warning. This container holds poisonous gas, and should only be opened and used by persons having expert knowledge of the precautions to be taken in its use."

If the poison is an arsenate, arsenite, copper acetoarsenite, halide of arsenic, organic compound of arsenic, oxide of arsenic, sodium thioarsenate, or sulphide of arsenic, and is intended for use in agriculture or horticulture for the destruction of bacteria, fungi, insects, vermin, or as weed-killer, it must be coloured with a distinctive water-soluble dye. This does not apply to lead arsenate paste or powder, poisons and sheep-dips which are themselves distinctively coloured, or articles to be exported to purchasers outside the United Kingdom.

- (v) place the substance in a container which is
  - (a) impervious to the poison and strong enough to prevent leakage from the ordinary risk of handling, and
  - (b) fluted vertically with ribs or grooves if the substance is a liquid supplied in a glass bottle of a capacity of 120 fluid ounces or less, and is not a medicine made up ready for the internal treatment of human ailments. Mouth-washes, eye-drops, eye-lotions, ear-drops, douches and similar articles are regarded as medicines for external use for the purpose of this provision.

(C) *Poisons not included in either the First or Fourth Schedules.*

The pharmacist must

- (i) label the poison with
  - (a) (i) the word "Poison" in the case of non-medicines, or medicines for external use (including mouth-washes, etc., as under (v) (b) above) or medicines for the internal treatment of human ailments not made up ready to be taken, or (ii) the words "Caution. It is dangerous to exceed the stated dose" in the case of medicines (other than those referred to under (iii) below)

which are made up ready for the internal treatment of human ailments, or (iii) the words "Caution. It is dangerous to take this preparation except under medical supervision" in the case of insulin, the active principles of pituitary gland, and the active principles of thyroid gland and their salts, if made up ready for the internal treatment of human ailments. The required word or words must appear either on a separate label or within a line containing no words other than the particulars with which the substance is required to be labelled by the Act or Rules, and must not be modified in meaning by other words or marks;

- (b) the particulars set out under *B* (iv) (a), (b), (c), (e) and (f) above (page 995), except that the name and address (*see* (a) ) need only appear on the outer cover of the article
- (ii) place the poison in a container as set out under (*B*) (v) above (page 997).

#### ***IV. Sales of poisons for use in business or profession.***

##### ***(A) Schedule 4 Poisons***

There are no special conditions which apply to the pharmacist in the sale or supply of Fourth Schedule poisons to a person requiring the poison for the purpose of his business or profession. All poisons in the Fourth Schedule with the exception of Sulphonal and Alkyl Sulphonals are, however, First Schedule poisons, and the normal requirements which apply to such poisons and described in the next paragraph must be observed.

##### ***(B) Poisons included in the First Schedule***

The purchaser must either attend in person to obtain the poison, or supply an order in writing signed by himself stating his name and address, his business or profession, the name and quantity of the article to be purchased and the purpose for which it is required. It is not necessary to state business or profession when the purchaser is a hospital, infirmary, dispensary or clinic.

The pharmacist must

- (i) satisfy himself
  - (a) that the poison is used in the business or profession of the purchaser, and
  - (b) that the purchaser is engaged in the business or profession stated, and
  - (c) if the purchaser does not attend in person, but supplies a written order, that the signature of the purchaser is genuine,
- (ii) comply with the conditions set out under ***III B*** above (pages 995 to 997). In sales or supplies to a person or

institution concerned with scientific education or research or chemical analysis, for the purposes of that education, research or analysis, the only requirement in regard to container is that it shall be impervious to the poison and strong enough to prevent leakage from the ordinary risk of handling.

See also note on Emergency (page 990).

(C) *Poisons not included in the First Schedule.*

The pharmacist must comply with the conditions set out under **B III** (C) (page 997 & 998).

### C. The wholesaler.

Subject to the proviso that a person who is carrying on a business which comprises the manufacture of medicines for the treatment of animals, and who has complied with the requirements of Rule 4 of the Poisons Rules, 1935, may sell or supply a poison as a medicine for the treatment of animals, a wholesaler may not sell or supply any poison direct to the public unless he is *either*

- (a) an authorised seller of poisons, in which case he must comply with the requirements set out in this summary under Section **B—The pharmacist** (page 993),
- or (b) a listed seller of poisons, in which case he may sell only certain poisons and must comply with the requirements affecting transactions by such persons. The requirements to be fulfilled by listed sellers of poisons are not set out in this summary.

Subject to the general prohibitions mentioned on page 989, any wholesaler who is not carrying on a retail business on the same premises may sell poisons as set out under sections **I to IV** below; transactions referred to under sections **V to IX** below may only be effected if in addition the wholesaler regularly sells poisons to purchasers who require them either to sell again or to use in their trade or business.

### I. To a purchaser (either wholesaler or retailer) who buys for the purpose of selling again.

(A) *Poisons included in the First Schedule.*

The wholesaler must

- (i) be satisfied that the purchaser requires the poison for the purpose of selling again;
- (ii) comply with the requirements set out under **B III** (B) (iv) and (v) (pages 995 to 997), subject to the proviso that no name and address is necessary if the poison is to be sold again in the same container, and the requirements of **B III** (B) (iv) (b) to (d) need not be satisfied if the poison is included in the Second Schedule, is sold to a wholesaler who carries on a business in the course of which poisons are either

regularly sold to purchasers who buy to sell again or regularly used in the manufacture of other articles, and who requires the poison for the purpose of that business, is labelled with the name of the seller and the address of the premises on which it is sold, and the outside of the package is labelled conspicuously with words indicating the dangerous properties of the poison.

*(B) Poisons not included in the First Schedule.*

The wholesaler must comply with the requirements set out under **B III (C) (i) and (ii)** (pages 997 & 998), subject to the proviso that no name and address is necessary if the poison is to be sold again in the same container, and the requirements of **B III (C) (i) (a) and B III (B) (iv) (a) to (c)** need not be satisfied if the poison is included in the Second Schedule, is sold to a wholesaler who carries on a business in the course of which poisons are either regularly sold to purchasers who buy to sell again or regularly used in the manufacture of other articles, and who requires the poison for the purpose of that business, is labelled with the name of the seller and the address of the premises on which it is sold, and the outside of the package is labelled conspicuously with words indicating the dangerous properties of the poison.

**II. To be exported to purchasers outside the United Kingdom.**

The requirements for all poisons, whether or not First Schedule, are the same; the wholesaler must comply with the requirements set out under **B III (B) (v) (a)** (page 997).

It will be noted that for export there are no requirements prescribed for labelling poisons, other than those for transport. Sales to Northern Ireland are not export sales, but such sales are exempt from the labelling requirements as set out under **B III (B) (iv)** (pages 995 to 997) and **B III (C) (i)** (pages 997 & 998), if the poisons are labelled in accordance with the laws of Northern Ireland.

**III. To a doctor, dentist, or veterinary surgeon for the purpose of their respective professions.**

The wholesaler must comply with the requirements as set out under **B IV** (page 998).

**IV. For use in or in connection with any hospital, infirmary, dispensary or similar institution approved by order, whether general or special, of the Secretary of State.**

(By the Poisons (Approved Institutions) Order, 1935, the Secretary of State has approved any hospital, infirmary or dispensary maintained by any public authority or out of any

public funds, or by a charity or by voluntary subscriptions.)

The wholesaler must comply with the requirements as set out under **B IV** (page 998).

**V. To a person who requires the poison for the purpose of his trade or business.**

**(A) Poisons included in the First Schedule.**

The wholesaler must

- (i) be satisfied that the purchaser requires the poison for the purpose of his trade or business;
- (ii) comply with the requirements set out under **B III (B) (iv) and (v)** (pages 995 to 997); except that
  - (a) if the poison is included in the Second Schedule, is sold to a wholesaler who carries on a business in the course of which poisons are either regularly sold to purchasers who buy to sell again or regularly used in the manufacture of other articles, and who requires the poison for the purpose of that business, is labelled with the name of the seller and the address of the premises on which it is sold, the requirements of **B III (B) (iv) (b) to (f)** need not be satisfied, provided the outside of the package is labelled conspicuously with words indicating the dangerous properties of the poison;
  - (b) if sold to a person concerned with chemical analysis a fluted bottle need not be used.

**(B) Poisons not included in the First Schedule.**

The wholesaler must comply with the conditions set out under **B III (C)** (page 997), except that

- (a) if the poison is included in the Second Schedule, is sold to a wholesaler who carries on a business in the course of which poisons are either regularly sold to purchasers who buy to sell again or regularly used in the manufacture of other articles and who requires the poison for the purpose of that business, the requirements of **B III (C) (i)** need not be satisfied, provided the requirements of **B III (B) (iv) (a)** are satisfied, and the outside of the package is labelled conspicuously with words indicating the dangerous properties of the poison;
- (b) if sold to a person concerned with chemical analysis a fluted bottle need not be used.

**VI. To a person who requires the poison for the purpose of enabling him to comply with any statutory requirements in respect of the medical treatment of his employees.**

The wholesaler must comply with the statutory requirements as set out under **B IV** (page 998).

**VII. *To a Government department or an officer of the Crown requiring the poison for the purposes of the public service.***

The wholesaler must comply with the requirements as set out under **B IV** (page 998).

**VIII. *To a local authority requiring the poison in connection with the exercise of statutory powers.***

The wholesaler must comply with the requirements as set out under **B IV** (page 998)

**IX. *To a person or institution concerned with scientific education or research if the poison is required for the purpose of that education or research.***

The wholesaler must comply with the requirements as set out under **B IV** (page 998), except that in no circumstances is it necessary to use a fluted bottle.

**D. Hospitals and similar institutions.**

***I. Out-patients.***

The ordinary rules governing the supply of poisons do not apply to any poison which is a medicine supplied for the treatment of human ailments from a hospital, infirmary or dispensary maintained by any public authority, or out of any public funds, or by a charity, or from any institution approved by the Minister of Health for the purpose of section 24 (4) of the National Health Insurance Act, 1924, or for the treatment of animals from a veterinary hospital which is under the superintendence of a veterinary surgeon, if the conditions set out below are satisfied.

(It will be noted that this does not authorise the *sale* of poisons "Sales" may only be effected if the institution becomes an authorised seller of poison within the meaning of the Pharmacy and Poisons Act, 1933.)

- (a) the medicine must not be supplied except by or on and in accordance with a prescription of a doctor, for the purposes of medical treatment, or a dentist for the purposes of dental treatment or a veterinary surgeon for the purposes of animal treatment,
- (b) if a First Schedule poison, a record must be kept on the premises so that at any time during the two years following the supply there can readily be traced the following particulars:—
  - (i) the name and quantity of the poison supplied,
  - (ii) the date of supply;
  - (iii) the name and address of the person supplied,
  - (iv) the name of the person who supplied the poison or who gave the prescription upon which it was supplied.

- These requirements need not be satisfied in the case of a National Health Insurance prescription.
- (c) The container of the medicine must be labelled
- (i) with a designation and address sufficient to identify the hospital or other institution from which it was supplied,
  - (ii) with the word "Poison" except in the case of a medicine made up ready for treatment;
  - (iii) with the words "For external use only" and the name of the article, *e g* , The Embrocation, The Liniment, etc., if the poison is a liquid for external application;
  - (iv) with the words "For animal treatment only" if the poison is supplied from a veterinary hospital;

## **II. In-patients.**

In any hospital, infirmary, dispensary, clinic, nursing-home, or other institution at which human ailments are treated, and in which medicines are dispensed in a separate dispensing or pharmaceutical department in charge of a person appointed for that purpose, no medicine containing a poison must be supplied from that department (except in cases of emergency) for use in the wards, operating theatres, or other sections of the institution unless

- (a) a written order signed by a doctor, dentist, or by a sister or nurse in charge of a ward, theatre or other section of the institution, is received; and
- (b) the container is labelled
  - (i) with words describing its contents;
  - (ii) in the case of First Schedule poisons with a distinguishing mark or other indication, indicating that the poison is to be stored in a cupboard reserved solely for the storage of poisons.

## **STORAGE OF POISONS.**

### **A. The doctor, dentist or veterinary surgeon.**

There are no regulations affecting the storage of poisons in the surgery of a doctor, dentist, or veterinary surgeon.

### **B. The pharmacist.**

With the exception of the general requirement that the container shall be impervious to the poison and stout enough to prevent leakage from ordinary risks of handling, only First Schedule poisons are affected by the provisions governing storage. Such poisons must be stored in manner set out below (but all three systems may be in use at the same time, and for the same substance):

- (i) in a cupboard or drawer reserved solely for the storage of poisons; or



- (ii) in a part of the premises which is partitioned off or otherwise separated from the remainder of the premises, and to which the public have not access; or
- (iii) on a shelf reserved solely for the storage of poisons; provided that
  - (a) no food is kept beneath the shelf; and
  - (b) the container of the poison is rendered distinguishable by touch from the containers of articles and substances other than poisons stored upon the same premises.

First Schedule poisons for use in agriculture or horticulture must be stored only in a cupboard or drawer reserved solely for such poisons or in accordance with (ii) above, provided that food is not kept in that part of the premises.

#### **C. The wholesaler, educational institutions and laboratories.**

There are no restrictions affecting the storage of poisons by wholesalers, educational institutions and laboratories, other than the general requirement that the container of the poison shall be impervious to the poison and stout enough to prevent leakage from the ordinary risks of handling.

#### **D. Hospitals and similar institutions.**

Under this heading, but for the purpose of storage only, is included any hospital, infirmary, dispensary, clinic, nursing-home, or other institution at which human ailments are treated.

##### *(i) Poisons not issued for use within the institution.*

- (a) If there is a dispensing department, poisons not issued for use within the institution must be stored in that department, but subject to any rules in the institution, the pharmacist may decide upon detail;
- (b) If there is no dispensing department, poisons not issued for use within the institution must be stored in charge of a person appointed for the purpose by the governing body or person in control of the institution, and if a First Schedule poison either in a cupboard, or drawer, or on a shelf reserved solely for the storage of poisons.

If a poison is stored on a shelf the container must be distinguishable by touch from the containers of articles other than poisons stored on the same premises.

##### *(ii) Poisons issued to the wards.*

Every First Schedule poison must be stored in a cupboard reserved solely for the storage of poisons and poisonous substances.

All places in which poisons are stored in hospitals and similar institutions must be inspected regularly, at intervals not exceeding three months, by a pharmacist or some other person appointed for the purpose by the governing body or person in control of the institution.

**TRANSPORT.**

All poisons consigned for transport must be sufficiently strongly packed to avoid leakage arising from the ordinary risks of handling and transport. In addition, poisons which are not medicines and are included in the Eighth Schedule, and which are consigned for transport by carrier, must be labelled conspicuously on the outside of the package with the name or description of the poison as set out in the Eighth Schedule, and a notice indicating that it is to be kept separate from food and from empty foodstuff containers.

It should also be noted that any poison in the First Schedule which is lawfully sold or supplied to any person on a written order must, if sent by post, be sent by registered post.

**MANUFACTURE.**

In all establishments in which pharmaceutical preparations containing poison are manufactured for the internal treatment of human ailments, the preparation must be manufactured by or under the supervision of a pharmacist, a Fellow or Associate of the Institute of Chemistry, or a person who for a period of at least three years before May 1, 1936, was continuously engaged in such manufacture, and has furnished to the Registrar of the Pharmaceutical Society of Great Britain a statement in writing, verified by a statutory declaration, to that effect, except that preparations containing pituitary, suprarenal or thyroid glands, their active principles or salts of their active principles, may be manufactured by or under the supervision of a doctor.

**THE POISONS LIST.****PART I (marked [P1] in our text)**

Acetanilide, alkyl acetanilides	Dihydromorphinone; its esters
Alkali fluorides other than those specified in Part II of this List	Ecgonine; its esters
Alkaloids, the following, their salts, simple or complex —	Emetine
Acetyldihydrocodeinone, its esters	Ephedra, alkaloids of
Aconite, alkaloids of	Ergot, alkaloids of
Apomorphine	Ethylmorphine
Atropine	Gelsemium, alkaloids of
Belladonna, alkaloids of	Homatropine
Benzoylmorphine	Hyoscine
Benzylmorphine	Hyoscyamine
Brucine	Jaborandi, alkaloids of
Calabar bean, alkaloids of	Lobelia, alkaloids of
Coca, alkaloids of	Morphine
Cocaine	Papaverine
Codeine	Pomegranate, alkaloids of
Colchicine	Quebracho, alkaloids of, other than the alkaloids of red quebracho
Coniine	Sabadilla, alkaloids of
Cotarnine	Solanaceous alkaloids not otherwise included in this List
Curarine	Stavesacre, alkaloids of
Diacetylmorphine	Strychnine
Dihydrocodeinone; its esters	Thebaine
Dihydrohydroxycodeinone, its esters	Veratrum, alkaloids of
Dihydromorphine; its esters	Yohimbe, alkaloids of
	Allylisopropylacetylurea

- Amidopyrine, its salts  
 Amino-alcohols, esterified with benzoic acid, phenylacetic acid, phenylpropionic acid, cinnamic acid or the derivatives of these acids  
 Amyl nitrite  
 Antimony, chlorides of; oxides of antimony, sulphides of antimony, antimonates; antimonites, organic compounds of antimony  
 Arsenical substances, the following, except those specified in Part II of this List—arsenic, halides of, oxides of arsenic, arsenates, arsenites, organic compounds of arsenic  
 Barbituric acid; its salts, derivatives of barbituric acid, their salts, compounds of barbituric acid, its salts, its derivatives, their salts, with any other substance  
 Barium, salts of, other than barium sulphate and the salts of barium specified in Part II of this List  
 Butyl chloral hydrate  
 Cannabis (the dried flowering or fruiting tops of *Cannabis sativa* Linn.); the resin of cannabis, extracts of cannabis, tinctures of cannabis; cannabin tannate  
 Cantharidin, cantharidates  
 Chloral formamide  
 Chloral hydrate  
 Chloroform  
 Creosote obtained from wood  
 Croton, oil of  
 Digitalis, glycosides of, other active principles of digitalis  
 Dinitrocresols, dinitronaphthols, dinitrophenols, dinitrothymols  
 Elaterin  
 Ergot (the sclerotia of any species of *Claviceps*), extracts of ergot, tinctures of ergot  
 Erythrityl tetranitrate  
 Glyceryl trinitrate  
 Guanidines, the following—polymethylene diguanidines, diparamisylphenetyl guanidine  
 Hydrocyanic acid; cyanides, double cyanides of mercury and zinc  
 Insulin  
 Lead acetates, compounds of lead with acids from fixed oils  
 Mannityl hexanitrate  
 Mercury, oxides of, nitrates of mercury, mercuric ammonium chlorides; potassio-mercuric iodides, mercuric oxycyanides, mercuric thiocyanate  
 Metanitrophenol, orthonitrophenol, paranitrophenol  
 Nux Vomica  
 Opium  
 Orthocaine, its salts  
 Quabain  
 Oxalic acid, metallic oxalates other than potassium quadroxalate  
 Oxycinchonic acid, derivatives of; their salts, their esters  
 Para-amino-benzoic acid, esters of, their salts  
 Phenetidylphenacetin  
 Phenols (any member of the series of phenols of which the first member is phenol and of which the molecular composition varies from member to member by one atom of carbon and two atoms of hydrogen) except in substances containing less than sixty per cent, weight in weight, of phenols, compounds of phenol with a metal, except in substances containing less than the equivalent of sixty per cent, weight in weight, of phenols  
 Phenylcinchoninic acid, salicylcinchonic acid, their salts, their esters  
 Phenylethylhydantoin, its salts, its acyl derivatives, their salts  
 Phosphorus, yellow  
 Picric acid  
 Picrotoxin  
 Pituitary gland, the active principles of  
 Savin, oil of  
 Strophanthus, glycosides of strophanthus  
 Sulphonal, alkyl sulphonals  
 Suprarenal gland, the active principles of; their salts  
 Thallium, salts of  
 Thyroid gland, the active principles of; their salts  
 Tribromethyl alcohol

## PART II (marked [P2] in our text).

- Ammonia  
 Arsenical substances, the following —  
 Arsenic sulphides  
 Arsenious oxide  
 Calcium arsenates  
 Calcium arsenites  
 Copper acetoarsenites  
 Copper arsenates  
 Copper arsenites  
 Lead arsenates  
 Potassium arsenites  
 Sodium arsenates  
 Sodium arsenites  
 Sodium thioarsenates  
 Barium, salts of, the following —  
 Barium carbonate  
 Barium silicofluoride  
 Formaldehyde  
 Hydrochloric acid  
 Hydrofluoric acid, potassium fluoride; sodium fluoride; sodium silicofluoride

Mercuric chloride, mercuric iodide, organic compounds of mercury	containing less than the equivalent of sixty per cent, weight in weight, of phenols
Nicotine, its salts	Phenylene diamines, toluene diamines, their salts
Nitric acid	Potassium hydroxide
Nitrobenzene	Potassium quadroxalate
Phenols as defined in Part I of this List in substances containing less than sixty per cent., weight in weight, of phenols; compounds of phenol with a metal in substances	Sodium hydroxide Sulphuric acid

(Note—Several poisons in this List are exempted by the Poisons Rules (Rule 11 and Third Schedule, pages 1009 to 1011), made by the Secretary of State under the Pharmacy and Poisons Act, 1933, from the application of the Act when present in certain specified substances or articles.)

### SCHEDULES TO THE POISONS RULES, 1935.

As amended April 24th, 1936

#### FIRST SCHEDULE (marked [81] in our text)

*Substances falling within the Poisons List, see pages 1005 to 1007, to which special restrictions apply*

Alkaloids, the following, their salts, simple or complex —

- Acetyldihydrocodeinone
- Aconite, alkaloids of, except substances containing less than 0.02 per cent of the alkaloids of aconite
- Apomorphine except substances containing less than 0.2 per cent of apomorphine
- Atropine except substances containing less than 0.15 per cent of atropine
- Belladonna, alkaloids of, except substances containing less than 0.15 per cent of the alkaloids of belladonna calculated as hyoscyamine
- Benzoylmorphine
- Benzylmorphine
- Brucine except substances containing less than 0.2 per cent of brucine
- Calabar bean, alkaloids of
- Coca, alkaloids of, except substances containing less than 0.1 per cent of the alkaloids of coca
- Cocaine except substances containing less than 0.1 per cent of cocaine
- Codeine except substances containing less than one per cent of codeine
- Colchicine except substances containing less than 0.5 per cent of colchicine
- Conine except substances containing less than 0.1 per cent of conine
- Cotarnine except substances containing less than 0.2 per cent of cotarnine
- Curarine
- Diacetylmorphine
- Dihydrocodeinone
- Dihydrohydroxycodeinone
- Dihydromorphine
- Dihydromorphinone
- Ecgonine except substances containing less than 0.1 per cent of ecgonine
- Emetine except substances containing less than one per cent of emetine
- Ergot, alkaloids of
- Ethylmorphine except substances containing less than 0.2 per cent. of ethylmorphine
- Gelsemium, alkaloids of, except substances containing less than 0.1 per cent of the alkaloids of gelsemium
- Homatropine except substances containing less than 0.15 per cent of homatropine
- Hyoscine except substances containing less than 0.15 per cent of hyoscine

- Hyoscyamine except substances containing less than 0·15 per cent. of hyoscyamine  
 Jaborandi, alkaloids of, except substances containing less than 0·5 per cent. of the alkaloids of jaborandi  
 Lobelia, alkaloids of, except substances containing less than 0·5 per cent. of the alkaloids of lobelia  
 Morphine except substances containing less than 0·2 per cent. of morphine calculated as anhydrous morphine  
 Nicotine  
 Papaverine except substances containing less than one per cent. of papaverine  
 Pomegranate, alkaloids of, except substances containing less than 0·5 per cent. of the alkaloids of pomegranate  
 Quebracho, alkaloids of  
 Sabadilla, alkaloids of, except substances containing less than one per cent. of the alkaloids of sabadilla  
 Solanaceous alkaloids, not otherwise included in this Schedule, except substances containing less than 0·15 per cent. of solanaceous alkaloids calculated as hyoscyamine  
 Stavesacre, alkaloids of, except substances containing less than 0·2 per cent. of the alkaloids of stavesacre  
 Strychnine except substances containing less than 0·2 per cent. of strychnine  
 Thebaine except substances containing less than one per cent. of thebaine  
 Veratrum, alkaloids of, except substances containing less than one per cent. of the alkaloids of veratrum  
 Yohimba, alkaloids of  
 Allylisopropylacetylurea  
 Amidopyrine; its salts  
 Amino-alcohols, esterified with benzoic acid, phenylacetic acid, phenylpropionic acid, cinnamic acid or the derivatives of these acids, except in substances containing less than ten per cent. of esterified amino-alcohols  
 Antimonial poisons except substances containing less than the equivalent of one per cent. of antimony trioxide  
 Arsenical poisons except substances containing less than the equivalent of 0·01 per cent. of arsenic trioxide  
 Barbituric acid; its salts, derivatives of barbituric acid; their salts; compounds of barbituric acid, its salts, its derivatives, their salts, with any other substance  
 Barium, salts of  
 Cannabis; the resin of cannabis, extracts of cannabis; tinctures of cannabis, cannabin tannate  
 Cantharidin except substances containing less than 0·01 per cent. of cantharidin  
 Cantharidates except substances containing less than the equivalent of 0·01 per cent. of cantharidin  
 Digitalis, glycosides of, except substances containing less than one unit of activity (as defined in the *British Pharmacopœia*) in two grammes of the substance  
 Dinitrocresols; dinitronaphthols; dinitrophenols, dinitrothymols  
 Ergot; extracts of ergot; tinctures of ergot  
 Guanidines, the following.—polymethylene diguanidines, dipara-anisylphenetyl guanidine  
 Hydrocyanic acid except substances containing less than 0·1 per cent. of hydrocyanic acid (HCN); cyanides except substances containing less than the equivalent of 0·1 per cent., weight in weight, of hydrocyanic acid (HCN); double cyanides of mercury and zinc  
 Lead, compounds of, with acids from fixed oils  
 Mercuric chloride except substances containing less than one per cent. of mercuric chloride, mercuric iodide except substances containing less than two per cent. of mercuric iodide; nitrates of mercury except substances containing less than the equivalent of three per cent., weight in weight, of mercury (Hg), potassio-mercuric iodides except substances containing less than the equivalent of one per cent. of mercuric iodide; organic compounds of mercury except substances containing less than the equivalent of 0·2 per cent., weight in weight, of mercury (Hg)  
 Metanitrophenol; orthonitrophenol; paranitrophenol  
 Nux Vomica except substances containing less than 0·2 per cent. of strychnine  
 Opium except substances containing less than 0·2 per cent. of morphine calculated as anhydrous morphine  
 Ouabain

Oxycinchoninic acid, derivatives of, their salts; their esters  
 Phenetidylphenacetin  
 Phenylcinchoninic acid; salicyl-cinchoninic acid; their salts; their esters  
 Phenylethylhydantoin; its salts; its acyl derivatives, their salts  
 Picrotoxin  
 Savin, oil of  
 Strophanthus, glycosides of  
 Thallium, salts of  
 Tribromethyl alcohol

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## SECOND SCHEDULE

*Poisons exempted by Rule 5 (2) from labelling provisions when sold or supplied in certain circumstances.*

Alkali fluorides  
 Ammonia  
 Antimony, chlorides of; oxides of antimony, sulphides of antimony; antimonates, antimonites  
 Chloroform  
 Dinitrocresols; dinitronaphthols, dinitrophenols  
 Formaldehyde  
 Glyceryl trinitrate  
 Hydrochloric acid  
 Hydrofluoric acid; sodium silicofluoride  
 Lead acetates, compounds of lead with acids from fixed oils  
 Mercuric chloride, mercuric iodide, organic compounds of mercury  
 Mercury, oxides of; nitrates of mercury  
 Metanitrophenol; orthonitrophenol; paranitrophenol  
 Nitric acid  
 Nitrobenzene  
 Oxalic acid, metallic oxalates  
 Phenols, compounds of phenol with a metal  
 Phosphorus, yellow  
 Picric acid  
 Potassium hydroxide  
 Sodium hydroxide  
 Sulphuric acid

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## THIRD SCHEDULE (marked [83] in our text).

*Articles exempted by Rule 11 from the provisions of the Act and of these Rules.*

## GROUP I.

## GENERAL EXEMPTIONS.

Adhesives, anti-fouling compositions; builders' materials; ceramics; distempers; electrical valves; enamels, explosives; fillers; fireworks; glazes; glue, lacquer solvents; loading materials; marking inks, matches; motor fuels and lubricants; paints other than pharmaceutical paints; photographic paper; pigments; plastics; polishes; printers' inks; propellants; rubber, varnishes.

## GROUP II.

## SPECIAL EXEMPTIONS.

<i>Poison.</i>	<i>Substance or article in which exempted.</i>
Acetanilide; alkyl acetanilides	Substances not being preparations for the treatment of human ailments
Alkaloids Emetine	Ipecacuanha; extracts and tinctures of ipecacuanha; substances containing less than 0.05 per cent. of emetine

Ephedra, alkaloids of	Substances containing less than one per cent of the alkaloids of ephedra
Jaborandi alkaloids of	Substances containing less than 0.025 per cent of the alkaloids of jaborandi
Lobelia, alkaloids of	Preparations for the relief of asthma in the form of cigarettes, smoking mixtures or fumigants, substances containing less than 0.1 per cent of the alkaloids of lobelia
Nicotine	Tobacco
Pomegranate, alkaloids of	Pomegranate bark
Solanaceous alkaloids	Stramonium contained in preparations for the relief of asthma in the form of cigarettes, smoking mixtures or fumigants
Stavesacre, alkaloids of	Soaps, ointments, lotions for external use
Ammonia	Substances not being solutions of ammonia or preparations containing solutions of ammonia, substances containing less than five per cent, weight in weight, of ammonia ( $\text{NH}_3$ ), refrigerators, smelling bottles
Arsenical poisons	Pyrites ores or sulphuric acid containing arsenical poisons as natural impurities
Chloroform	Substances containing less than ten per cent of chloroform
Creosote obtained from wood	Substances containing less than fifty per cent of creosote obtained from wood
Dinitrophenols	Substances not being preparations for the treatment of human ailments
Formaldehyde	Substances containing less than five per cent, weight in weight, of formaldehyde ( $\text{HCHO}$ ), photographic glazing or hardening solutions
Hydrochloric acid	Substances containing less than nine per cent, weight in weight, of hydrochloric acid ( $\text{HCl}$ )
Lead acetate	Substances containing less than four per cent of lead acetate
Lead, compounds of	Machine-spread plasters
Mercuric chloride	Batteries
Mercuric chloride, mercuric iodide, organic compounds of mercury	Dressings on seeds or bulbs
Mercury, nitrates of	Ointments containing less than the equivalent of three per cent, weight in weight, of mercury ( $\text{Hg}$ )
Nitric acid	Substances containing less than nine per cent, weight in weight, of nitric acid ( $\text{HNO}_3$ )
Nitrobenzene	Substances containing less than 0.1 per cent of nitrobenzene, soaps containing less than one per cent. of nitrobenzene
Phenols	Carvacrol; coal tar, crude or refined, creosote obtained from coal tar, essential oils in which phenols occur naturally, medicines containing less than one per cent of phenols, nasal sprays, mouth-washes, pastilles, lozenges, capsules, pessaries, ointments, or suppositories containing less than 2.5 per cent. of phenols; smelling bottles, soaps for washing, solid substances containing less than sixty per cent of phenols; tertiary butyl-cresol; thymol
Phenylene diamines, toluene diamines, their salts	Substances other than preparations for the dyeing of hair.
Picric acid	Substances containing less than five per cent. of picric acid

Potassium hydroxide	Substances containing less than twelve per cent of potassium hydroxide, accumulators, batteries
Sodium fluoride	Substances containing less than three per cent of sodium fluoride as a preservative
Sodium hydroxide	Substances containing less than twelve per cent of sodium hydroxide
Sodium silicofluoride	Substances containing less than three per cent of sodium silicofluoride as a preservative
Sulphuric acid	Substances containing less than nine per cent, weight in weight, of sulphuric acid ( $H_2SO_4$ ), accumulators, batteries, fire extinguishers.

## FOURTH SCHEDULE (marked [84] in our text)

*Substances required by Rule 12 to be sold by retail only upon a prescription given by a qualified medical practitioner, registered dentist or registered veterinary surgeon.*

Amidopyrine, its salts  
 Barbituric acid, its salts, derivatives of barbituric acid, their salts, compounds of barbituric acid, its salts, its derivatives, their salts, with any other substance  
 Dinitrocresols, dinitronaphthols, dinitrophenols, dinitrothymols  
 Phenylcinchoninic acid, salicyl-cinchoninic acid, their salts, their esters  
 Sulphonal, alkyl sulphonals

## FIFTH SCHEDULE

*Form to which the substances specified are restricted when sold by listed sellers of Part II poisons (Rule 14 (2) (a) )*

<i>Poison</i>	<i>Form to which sale is restricted</i>
Arsenical substances—	
Arsenous oxide	Sheep dips, sheep washes
Arsenic sulphides	" " " "
Calcium arsenates	Agricultural and horticultural insecticides or fungicides
Calcium arsenites	" " " "
Copper acetoarsenite	" " " "
Copper arsenates	" " " "
Copper arsenites	" " " "
Lead arsenates	" " " "
Potassium arsenites	Sheep dips, sheep washes
Sodium arsenates	" " " "
Sodium arsenites	" " " "
Sodium thioarsenates	" " " "
Barium carbonate	Preparations for the destruction of rats and mice
Mercurial substances—	
Mercuric chloride	Agricultural and horticultural fungicides, seed and bulb dressings, insecticides
Mercuric iodide	Agricultural and horticultural fungicides, seed and bulb dressings
Organic compounds of mercury	" " " "
Nitrobenzene	Agricultural and horticultural insecticides, substances for the treatment of bee disease



## SIXTH SCHEDULE (marked [86] in our text).

*Statement of particulars as to proportion of the poison in certain cases permitted by Rule 18 (2)*

<i>Name of Poison.</i>	<i>Particulars.</i>
Alkaloids	The proportion of any one alkaloid of aconite that the preparation would be calculated to contain on the assumption that all the alkaloids of aconite in the preparation were that alkaloid.
Aconite, alkaloids of	The same as above, with the substitution for the reference to aconite of a reference to belladonna, calabar bean or such other of the said poisons as the case may require.
Belladonna, alkaloids of	
Calabar bean, alkaloids of	
Coca, alkaloids of	
Ephedra, alkaloids of	
Ergot, alkaloids of	
Gelsemium, alkaloids of	
Jaborandi, alkaloids of	
Lobelia, alkaloids of	
Pomegranate, alkaloids of	
Quebracho, alkaloids of, other than the alkaloids of red quebracho	
Sabadilla, alkaloids of	
Solanaceous alkaloids not otherwise included in the Poisons List.	
Stavesacre, alkaloids of	
Veratrum, alkaloids of	
Yohimba, alkaloids of	
Antimonial poisons	The proportion of antimony trioxide ( $\text{Sb}_2\text{O}_3$ ) or antimony pentoxide ( $\text{Sb}_2\text{O}_5$ ) that the preparation would be calculated to contain on the assumption that the antimony (Sb) in the poison had been wholly converted into antimony trioxide or antimony pentoxide as the case may be.
Arsenical poisons	The proportion of arsenic trioxide ( $\text{As}_2\text{O}_3$ ) or arsenic pentoxide ( $\text{As}_2\text{O}_5$ ) that the preparation would be calculated to contain on the assumption that the arsenic (As) in the poison had been wholly converted into arsenic trioxide or arsenic pentoxide as the case may be.
Barium, salts of	The proportion of one particular barium salt which the preparation would be calculated to contain on the assumption that the barium (Ba) in the poison had been wholly converted into that salt.
Digitalis, glycosides of; other active principles of digitalis	The number of units of activity as defined in the <i>British Pharmacopœia</i> contained in a specified quantity of the preparation
Hydrocyanic acid; cyanides, double cyanides of mercury and zinc	The proportion of hydrocyanic acid (HCN) that the preparation would be calculated to contain on the assumption that the cyanides in the poison had been wholly converted into hydrocyanic acid.
Lead, compounds of, with acids from fixed oils	The proportion of lead oxide ( $\text{PbO}$ ) that the preparation would be calculated to contain on the assumption that the lead in the poison had been wholly converted into lead oxide.
Mercury, organic compounds of	The proportion of organically-combined mercury (Hg) contained in the preparation.
Phenols	The proportion of phenols (added together) contained in the preparation.
Compounds of phenol with a metal	The proportion of phenols (added together) that the preparation would be calculated to

Pituitary gland, the active principles of	<p>contain on the assumption that the compounds of phenols with a metal had been wholly converted into the corresponding phenols.</p> <p>Either—</p> <ul style="list-style-type: none"> <li>(a) the number of units of activity as defined in the <i>British Pharmacopœia</i> contained in a specified quantity of the preparation, or</li> <li>(b) the proportion of pituitary gland, or of anterior or of posterior lobe of the gland, as the case may be, contained in the preparation, or</li> <li>(c) the amount of pituitary gland, or of anterior or of posterior lobe of the gland, as the case may be, from which a specified quantity of the preparation was obtained, together with an indication whether the amount relates to fresh or to dried gland substance.</li> </ul>
Potassium hydroxide	<p>The proportion of potassium monoxide (<math>K_2O</math>) which the preparation would be calculated to contain on the assumption that the potassium hydroxide in the preparation had been wholly converted into potassium monoxide.</p>
Sodium hydroxide	<p>The proportion of sodium monoxide (<math>Na_2O</math>) which the preparation would be calculated to contain on the assumption that the sodium hydroxide in the preparation had been wholly converted into sodium monoxide.</p>
Strophanthus, glycosides of	<p>The amount of Standard Tincture of Strophanthus as defined in the <i>British Pharmacopœia</i> which possesses the same activity as a specified quantity of the preparation when assayed by the method described in the said <i>Pharmacopœia</i></p>
Suprarenal gland, the active principles of; their salts	<p>Either—</p> <ul style="list-style-type: none"> <li>(a) the proportion of suprarenal gland or of the cortex or of the medulla of the gland, as the case may be, contained in the preparation, or</li> <li>(b) the amount of suprarenal gland, or of the cortex or of the medulla of the gland, as the case may be, from which a specified quantity of the preparation was obtained, together with an indication whether the amount relates to fresh or to dried gland substance.</li> </ul>
Thyroid gland, the active principles of, their salts	<p>Either—</p> <ul style="list-style-type: none"> <li>(a) the proportion of thyroid gland contained in the preparation, or</li> <li>(b) the amount of thyroid gland from which a specified quantity of the preparation was obtained together with an indication whether the amount relates to fresh or to dried gland.</li> </ul>

SEVENTH SCHEDULE (marked [87] in our text, except substances to which clause 2 of this schedule applies).

Indication of character prescribed by Rule 19 for the purposes of section 18 (1) (c) (iii) of the Act.

1. To be labelled with the words "*Caution It is dangerous to take this preparation except under medical supervision.*"—

Medicines made up ready for the internal treatment of human ailments if the poison is one of the following:—

Allylisopropylacetylurea

Insulin

Phenylethylhydantoin, its salts, its acyl derivatives, their salts

Pituitary gland, the active principles of

Thyroid gland, the active principles of, their salts

2 To be labelled with the words "*Caution It is dangerous to exceed the stated dose*" —

Medicines (other than medicines mentioned in paragraph 1 of this Schedule) made up ready for the internal treatment of human ailments except in the case of a substance included in the First Schedule

3 To be labelled with the words "*Poison. For animal treatment only.*" —  
Medicines made up ready for the treatment of animals

4 To be labelled with the words "*Caution. This preparation may cause serious inflammation of the skin in certain persons and should be used only in accordance with expert advice.*" —

Preparations for the dyeing of hair containing phenylene diamines or toluene diamines or their salts.

5 To be labelled with the words "*Caution. This substance is caustic.*" :—  
Potassium hydroxide, sodium hydroxide, and articles containing either of those substances

#### EIGHTH SCHEDULE

*Poisons to which Rule 25 (Transport) applies*

Arsenical poisons

Barium, salts of

Hydrocyanic acid, cyanides

Nicotine

Strychnine

Thallium, salts of

#### NINTH SCHEDULE

*Form of application to be made to the local authority by a person desiring his name to be entered in the list kept by local authorities in pursuance of section 21 of the Act (Rule 30 (1))*

#### PHARMACY AND POISONS ACT, 1933

*Form of application by a person to have his name entered in a local authority's list of persons entitled to sell poisons included in Part II of the Poisons List*

To the { Town Clerk  
          { Clerk of the County Council } of

I, . . . . .

being engaged in the business of

hereby apply to have my name entered in the list kept in pursuance of section 21 of the above Act in respect of the following premises, namely, . . . . .

.... . . . . .

.... . . . . .

.... . . . . .

as a person entitled to sell from those premises poisons included in Part II of the Poisons List.

I hereby nominate

..... . . . .

to act as my deputy (deputies) for the sale of poisons in accordance with Rule 14 (1) of the Poisons Rules.

Signature of applicant . . . . .

Date . . . . .

(The following note to be set out on the form )

# NOTE.

The entry of a person's name on a local authority's list does not entitle that person to retail poisons in Part I of the Poisons List which, by the provisions of the Act, may only be retailed by authorised sellers of poisons (i.e. registered pharmacists)

A person whose name is entered in a local authority's list (a listed seller of Part II poisons) is permitted, *subject to certain conditions* (see below), to sell the poisons in Part II of the Poisons List, namely —

Ammonia, arsenic sulphides; arsenious oxide, calcium arsenates; calcium arsenites, copper acetoarsenites, copper arsenates, copper arsenites, lead arsenates, potassium arsenites, sodium arsenates, sodium arsenites, sodium thioarsenates, barium carbonate, barium silicofluoride, formaldehyde, hydrochloric acid (spirits of salt), hydrofluoric acid, potassium fluoride, sodium fluoride, sodium silicofluoride, mercuric chloride, mercuric iodide, organic compounds of mercury, nicotine and its salts, nitric acid, nitrobenzene, phenols (carbolic acid and its homologues) in substances containing less than sixty per cent, weight in weight, of phenols; compounds of phenol with a metal in substances containing less than the equivalent of sixty per cent, weight in weight, of phenol, phenylene and toluene diamines and their salts (hair dyes), potassium hydroxide (caustic potash), potassium quadroxalate (salts of lemon), sodium hydroxide (caustic soda), sulphuric acid

The requirements which apply to the sale of poisons by a listed seller of Part II poisons are laid down in section 18 of the Act and in the Poisons Rules.

The following is a summary of the requirements —

## A.—Requirements applying to all listed sellers of Part II poisons.

1. The sale must be effected on the premises specified in the local authority's list

2. The container of the poison must be labelled with the various particulars and in the manner required by section 18 (1) (c) of the Act and Rules 16 to 21

3. No poison may be sold except in containers which comply with the requirements of Rule 22.

4. In the case of any arsenical or mercurial substance (unless it contains no more than the small proportions of arsenic or mercury specified in the First Schedule to the Poisons Rules), and in the case of barium silicofluoride and nicotine, the purchaser must either (a) be known to the seller, or to the person in charge of the premises on which the substance is sold or of the department of the business in which the sale is effected, to be a person to whom the poison may properly be sold or (b) produce a valid certificate in the form prescribed in the Eleventh Schedule to the Rules. In addition, in the case of such poisons, the required particulars of the sale must be entered, before delivery, in the Poisons Book to be kept in the form prescribed in the Twelfth Schedule to the Rules and (subject to the exception next mentioned) the entry must be signed by the purchaser (Rule 6.) In the case of a sale to a person for the purpose of his trade or business (farmer, horticulturist, etc.), Rule 7 (3) permits his signature of the entry in the Poisons Book to be dispensed with upon certain conditions, one of which is that an order signed by the purchaser has previously been obtained

5. Arsenical and mercurial substances, barium carbonate and nitrobenzene may be sold only in particular types of preparation as specified in the Fifth Schedule to the Rules (e.g. sodium arsenates in sheep dips, calcium arsenates in insecticides), and in containers labelled clearly with a notice of the special purpose for which they are to be used and with a warning that they are to be used for that purpose only. (Rule 14 (2) (a) )

6. No arsenical substance (other than lead arsenates, calcium arsenates and copper acetoarsenites), nor mercurial substances may be sold to private persons; such substances may be sold only to persons engaged in the trade or business of agriculture or horticulture and for the purpose of that business (Rule 14 (2) (b) )

7. It is unlawful to store any poison except in a container impervious to the poison and sufficiently stout to prevent leakage from the container arising from the ordinary risks of handling (Rule 23 (1) )

8. Any poison consigned for transport must be sufficiently stoutly packed to avoid leakage arising from the ordinary risks of handling and transport

The outside of the package of any arsenical poison, salts of barium or nicotine consigned for transport by a carrier must be labelled conspicuously with the name of the poison and a notice indicating that it is to be kept separate from food and from empty containers in which food has been contained, and no such poison may be knowingly transported in any vehicle in which food is being transported unless the food is carried in a part of the vehicle effectively separated from that containing the poison, or is otherwise adequately protected from the risk of contamination. (Rule 25.)

**B.—Additional requirements applying solely to listed shopkeepers.**

1. No poison, other than ammonia, hydrochloric acid (spirits of salt), nitric acid, potassium quadroxalate (salts of lemon) and sulphuric acid, may be sold by a listed shopkeeper except in closed containers as closed by the manufacturer or other person from whom the poison was obtained. (Rule 14 (1) (a).)

2. Arsenical or mercurial substances (unless they contain no more than the small proportions of arsenic or mercury specified in the First Schedule to the Rules), barium silicofluoride and nicotine may not be sold except by the listed shopkeeper himself or by a responsible deputy nominated by him to the local authority in accordance with Rule 14 (1) (b).

3. Arsenical and mercurial substances (unless they contain no more than the small proportions of arsenic or mercury specified in the First Schedule to the Rules) and nicotine may not be stored on a shelf, but must be stored in a cupboard or drawer reserved solely for the storage of poisons to be used in agriculture or horticulture, or in a part of the premises which is partitioned off or otherwise separated from the remainder of the premises, to which customers are not permitted to have access and in which no food is kept.

Barium silicofluoride must be stored either in a cupboard, drawer or shelf reserved solely for the storage of poisons, or in a part of the premises which is partitioned off or otherwise separated from the remainder of the premises and to which customers are not permitted to have access. If barium silicofluoride is kept on a shelf no food may be kept directly under the shelf and the container of the substance must be rendered distinguishable by touch from the containers of articles and substances other than poisons stored upon the same premises. (Rule 23 (2).)

## TENTH SCHEDULE.

*Form of the list to be kept by local authorities in pursuance of section 21 (1) of the Act. (Rule 30 (3).)*

### PHARMACY AND POISONS ACT, 1933.

List of persons entitled to sell poisons in Part II of the Poisons List.

Full Name.	Address of Premises.	Description of business carried on at the premises.	Name of Deputy (or deputies) permitted to sell.

## ELEVENTH SCHEDULE.

*Certificate for the purchase of a poison. (Rule 31.)*

For the purposes of subsection (2) (a) (i) of section 18 of the Pharmacy and Poisons Act, 1933, I, the undersigned, a householder occupying (a)

. . . hereby certify from my knowledge of (b)  
of (a) that he is a person to whom (c)  
may properly be supplied

I further certify that (d) is the signature of the  
said (b)

Signature of householder giving  
certificate

Date

- (a) Insert full postal address
- (b) Insert full name of intending purchaser
- (c) Insert name of poison
- (d) Intending purchaser to sign his name here

*Endorsement required by Rule 31 of the Poisons Rules to be made by a police officer in charge of a police station, when, but only when, the householder giving the certificate is not known to the seller of the poison to be a responsible person of good character.*

I hereby certify that in so far as is known to the police of the district in which\* . . . resides he is a responsible person of good character

Signature of Police Officer .

Rank .

In charge of Police Station at

Date .

Office Stamp of  
Police Station.

\* Insert full name of householder giving the certificate



**PHARMACY AND POISONS ACT (NORTHERN IRELAND), 1926.**  
**Schedule of Poisons Applicable to Northern Ireland**  
*(as amended to October, 1936)*

**PART I.**

**Aconite, Aconitine** and their preparations.

**Alkaloids.**—All poisonous alkaloids not specifically named in this Schedule, and their salts, and all poisonous derivatives of alkaloids

**Arsenic** and its preparations

**Atropine** and its salts and their preparations

**Belladonna** and all preparations or admixtures (except belladonna plasters) containing 0·1 or more per cent. of belladonna alkaloids.

**Cannabis**, the dried flowering or fruiting tops of the pistillate plant of *C. sativa*, and the resins prepared therefrom

**Cantharides** and its poisonous derivatives

**Chloral Hydrate** and all its preparations.

**Coca**, any preparation or admixture of, containing 0·1 or more per cent. of coca alkaloids

**Corrosive Sublimate** and preparations of corrosive sublimate

**Cyanide of Potassium** and all poisonous cyanides and their preparations

**Diamorphine** (also known as **Heroin**) and all preparations or admixtures containing 0·1 per cent. of diamorphine.

**Diethyl-Barbituric Acid** and other alkyl, aryl or metallic derivatives of barbituric acid, whether described as Veronal, Proponal, Medinal, or by any other trade name, mark or designation, and all poisonous urethanes and ureides.

**Digitalin** and all other poisonous constituents of digitalis

**Dinitro Phenols, Dinitro Cresols**, preparations or admixtures containing dinitro phenols, preparations or admixtures containing dinitro cresols

**Ecgonine** and all preparations and admixtures containing 0·1 per cent. of ecgonine

**Emetic Tartar** and all preparations or admixtures containing 1 or more per cent. of emetic tartar.

**Ergot of Rye** and preparations of ergots

**Lead**, in combination with oleic acid, or other higher fatty acids, whether sold as Diachylon or under any other designation (except machine-spread plasters)

**Nux Vomica** and all preparations or admixtures containing 0·2 or more per cent. of strychnine

**Opium** and all preparations or admixtures containing 0·2 or more per cent. of morphine

**Phenylcinchoninic Acid**, its salts, its esters; derivatives of phenylcinchoninic acid, their salts, their esters, preparations and admixtures containing phenylcinchoninic acid, its salts, its esters, preparations and admixtures containing derivatives of phenylcinchoninic acid, their salts, their esters.

**Picrotoxin.**

**Prussic Acid** and all preparations or admixtures containing 0·1 or more per cent. of prussic acid

**Savin** and its oil, and all preparations or admixtures containing savin or its oil.

**Strophanthin** and all other poisonous constituents of strophanthus

**Sulphuric Ether.**

**Tobacco**, any preparations or admixtures of (except tobacco prepared for smoking and snuff), containing the poisonous alkaloids of tobacco

**PART II.**

**Almonds, Essential Oil of** (unless deprived of prussic acid)

**Antimonial Wine.**

**Barium, Salts of**, except barium sulphate

**Cantharides**, tincture and all vesicating liquid preparations or admixtures of

**Carbolic Acid**, and liquid preparations of carbolic acid, and its homologues containing more than 3 per cent. of those substances

**Chloroform** and all preparations or admixtures containing more than 20 per cent. of chloroform.

**Digitalis.**

**Mercury, Ammoniated (White Precipitate).**

**Mercury, Biniodide (Mercuric Iodide).**

**Mercury, Red Oxide (Red Precipitate)** and all oxides of.

**Mercuric Sulphocyanide.**

**Oxalic Acid.**

**Phosphorus** and all preparations and admixtures containing it in a free state (except lucifer matches).



**Poppies**, all preparations of, except red poppy petals and syrup of red poppies (*Papaver rhæas*).

**Strophanthus**.

**Sulphonal** and its homologues, whether described as Trional, Tetronal or by any other trade mark, name or designation.

**Zinc Chloride** and liquid preparations of zinc chloride, except preparations intended to be used for soldering, or other purely industrial purpose, provided that they are contained in closed vessels labelled with the word "Poisonous," and bearing the name and address of the seller and a notice of the special purpose for which the preparations are intended.

All preparations or admixtures which are not included in Part I of this Schedule, and contain a poison within the meaning of this Act, except tobacco prepared for smoking and snuff, machine-spread lead plasters, preparations or admixtures the exclusion of which from this Schedule is indicated by the words therein relating to chloroform, and except such substances as come within the provisions of Section 5 of the Poisons and Pharmacy Act, 1908.

**SALE OF POISONS (IRELAND) ACT, 1870.**  
**Schedule of Poisons Applicable to Irish Free State**  
*(as amended to October, 1936)*

**PART I.**

**Aconite** and its preparations.

**Alkaloids**, *see* Strychnine.

**Arsenic** and its preparations.

**Cantharides**.

**Coca**, any preparation or admixture of, containing 1 or more per cent of coca alkaloids.

**Corrosive Sublimate**.

**Cyanide of Potassium** and all metallic cyanides

**Diamorphine** (also known as heroin) and all preparations or admixtures containing 0.1 per cent. of diamorphine

**Ecgonine** and all preparations or admixtures containing 0.1 per cent. of ecgonine.

**Emetic Tartar**.

**Ergot of Rye** and its preparations

**Opium** and all preparations or admixtures containing 0.2 or more per cent of morphine.

**Prussic Acid**.

**Savin** and its oil.

**Strychnine** and all poisonous vegetable alkaloids and their salts.

**PART II.**

**Almonds, Essential Oil of**, unless deprived of its prussic acid.

**Ammoniated Mercury**.

**Belladonna** and its preparations

**Cantharides**, the tincture and all vesicating liquid preparations of.

**Carbolic Acid**, *see* Phenol.

**Chloral Hydrate** and all its preparations

**Chloroform**.

**Corrosive Sublimate**, preparations of.

**Diethyl Barbituric Acid** and other alkyl, aryl, or metallic derivatives of barbituric acid, whether described as Veronal, Proponal, Medinal or by any other trade name, mark or designation, and all poisonous urethanes and ureides

**Ether, Sulphuric**

**Mercury, Biniiodide of**.

**Mercury, Red Oxide of**.

**Morphine**, preparations of

**Nux Vomica** and its preparations.

**Opium** and all preparations of opium or poppies.

**Oxalic Acid** and all oxalates.

**Phenol**, commonly called carbolic acid, and its homologues containing not more than nine carbon atoms, and all preparations and admixtures thereof, except tooth-pastes, tooth-powders and soaps for washing.

**Phosphorus** and all preparations containing it in a free state.

**Poppies**, all preparations of, *see* Opium.

**Strychnine**, preparations of.

**Every Compound** containing any of the poisons mentioned in this Schedule when prepared or sold for the destruction of vermin.

**SUMMARY OF DANGEROUS DRUGS LEGISLATION****Main Points to Remember in Prescribing and Dispensing**

The drugs (marked [D] in our text) to which the Acts apply are set out on page 1023 & 1024.

For exempted preparations *see* page 1030.

***Specimen form of prescription for "dangerous drugs."*****1. Doctor.**

[Address of prescriber]*
[Name and address of patient.]
[Name and quantity of ingre- dients, including dose and total amount of finished product to be supplied]
[To be repeated X times]†
[Date]
[Signature (not initials) of prescriber].

**2. Dentist.**

As above, but in addition the words "For local dental treatment only" must be written on the prescription.

**3. Veterinary Surgeon.**

As for doctor's prescription except that the "name and address of the person to whom the medicine is to be delivered" must be inserted in place of the "name and address of patient," and the words "For animal treatment only" must be written on the prescription

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\*Address of doctor is not necessary in the case of National Health Insurance prescriptions.

†If not to be repeated, this entry should be omitted. The maximum number of times which a prescription may be ordered to be repeated is two (*i.e.*, it may be dispensed three times in all). If desired, the prescriber may state the actual dates upon which the medicine may be repeated; he may also indicate what period of time should elapse before repeating on any occasion.

***When dispensing a prescription the pharmacist must***

- (i) know the signature of the prescriber;
- (ii) be satisfied that the prescription is genuine. He should make sure if possible that the doctor, dentist, or veterinary surgeon is authorised to prescribe "dangerous drugs",
- (iii) mark the prescription with the date on which it is dispensed,
- (iv) retain the prescription for two years,
- (v) make the required records in the "dangerous drugs" register on the same or following day on which the prescription is dispensed,
- (vi) make a copy of the prescription in the prescription book

***Sales to doctors, dentists, and veterinary surgeons***

The requirements in regard to sales of First Schedule poisons, set out on page 998, must be complied with and, in addition, records must be made in the "dangerous drugs" register

**SPECIMEN FORM OF "SIGNED ORDER" OF DOCTOR, DENTIST  
AND VETERINARY SURGEON.**

Please supply —

[Name and quantity of drugs required ]

[These drugs are required for use in my medical\* practice ]

[Signature (not initials) of practitioner ]

***Other points of assistance***

All dangerous drugs must be kept in a locked receptacle, the key being kept only by a pharmacist

All dangerous drugs are [P1 81] poisons

Dentists' and veterinary surgeons' (not doctors') prescriptions must have the amount of the dangerous drug stated on the label

Typewritten prescriptions are accepted as written

Doctors may write prescriptions for themselves.

Telephone orders from medical practitioners may be accepted, but the written order must follow within twenty-four hours

Nursing homes are not authorised persons

A foreign doctor, dentist, or veterinary surgeon is not authorised to prescribe, or be in possession of, dangerous drugs unless he is registered in Great Britain

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\*A dentist should replace the word "medical" with the word "dental," and a veterinary surgeon with the word "veterinary."

## DANGEROUS DRUGS ACT, 1920, SUMMARISED.

(10 AND 11 GEO. V, CHAPTER 46.)

*With the amendments of the 1923, 1925 and 1932 Acts incorporated.***[D]** *Throughout our pages means drugs or preparations coming within the provisions of these Acts**In this Summary "medical practitioner" means "duly qualified," i. e., registered in the Medical Register kept by the General Medical Council, 44 Hallam Street, London, W 1, "dentist" means "registered dentist", "veterinary surgeon" means "registered veterinary surgeon"*

**PART I.—Raw Opium, Coca Leaves and Indian Hemp.** Sections 1 to 3 prohibit, except under licence and at approved ports, the importation into and exportation from the United Kingdom of raw opium, coca leaves, Indian hemp, resins obtained from Indian hemp and all preparations of which such resins form the base. Where the importation of any of the above-named drugs is prohibited in any foreign country, the Secretary of State may make such conditions in regard to the licence as he deems necessary to prevent exportation from the United Kingdom to that foreign country. The Secretary of State is also empowered to make regulations controlling the production, possession, sale and distribution of these drugs. A summary of these regulations appears on pages 1032 to 1033.

**PART II.—Prepared Opium.** Section 4—Import and export totally and unconditionally prohibited. Section 5—Any person manufacturing, selling, dealing in, or having in possession prepared opium, or being occupier of premises used for preparation of opium for smoking, or sale or smoking of prepared opium, or being concerned in managing premises so used, or having pipes or utensils for smoking opium or preparing opium for smoking, or smoking or otherwise using prepared opium, or frequenting a place used for smoking, is guilty of offence against this Act.

**PART III.—Cocaine, Morphine, etc.** (as detailed in Section 8 below)  
Section 6—Import and export prohibited, except under licence

Section 7. Sub-section 1—Provides for the making of regulations controlling the manufacture, sale, possession and distribution of drugs to which this part (Part III) of this Act applies. Sub-section 2—The regulations so made shall provide for authorising any person lawfully carrying on a chemist's business (a) to manufacture at the shop in the ordinary course of his retail business any preparation, admixture or extract of any drug to which this Part of this Act applies; or (b) to carry on at the shop the business of retailing, dispensing or compounding any such drug. This authorisation shall be subject to the power of the Secretary of State, after consulting the Council of the Pharmaceutical Society of Great Britain, withdrawing it from any person convicted of an offence under this Act. Sub-section 3—Nothing in the regulations made under this section shall derogate from the provisions of the Pharmacy Act, 1868, as amended.

Section 8. Sub-section 1—The drugs to which this part of the Act applies are

- (a) medicinal opium,
- (b) any extract or tincture of Indian hemp,
- (c) morphine and its salts, and diacetylmorphine (commonly known as diamorphine or heroin) and the other esters of morphine and their respective salts,
- (d) cocaine (including synthetic cocaine) and ecgonine and their respective salts, and the esters of ecgonine and their respective salts,
- (e) any solution or dilution of morphine or cocaine or their salts in an inert substance, whether liquid or solid, containing any proportion of morphine or cocaine, and any preparation, admixture, extract or other substance (not being such a solution or dilution as aforesaid) containing not less than one-fifth per cent of morphine or one-tenth per cent. of cocaine or of ecgonine;
- (f) any preparation, admixture, extract or other substance containing any proportion of diacetylmorphine,
- (g) dihydroxycodeinone, dihydrocodeinone, dihydromorphinone, acetyl-dihydrocodeinone, dihydromorphine, their esters and the salts of any of these substances and of their esters, morphine-N-oxide (commonly known as genomorphine), the morphine-N-oxide derivatives, and any other pentavalent nitrogen morphine derivatives,

- (h) thebaine and its salts, and (with the exception of methylmorphine, commonly known as codeine, and ethylmorphine, commonly known as dionin, and their respective salts†) benzylmorphine and the other ethers of morphine and their respective salts;
- (i) any preparation, admixture, extract or other substance containing any proportion of any of the substances mentioned in paragraph (g) or in paragraph (h) of this sub-section.

For the purpose of the foregoing provision the expression "ecgonine" means lævo-ecgonine, and includes any derivatives of ecgonine from which it may be recovered industrially, and the percentage in the case of morphine shall be calculated as in respect of anhydrous morphine.

*Sub-section 2.*—By Order in Council this part of the Act may be applied to new derivatives of morphine, cocaine, or any other substance.

#### **PART IV.—General. Section 9.—Application of Customs Acts.**

*Section 10. Sub-section 1.*—A constable or person authorised by a Secretary of State has power to inspect books or documents relating to dealings and stocks. *Sub-section 2.*—Any person delaying, or obstructing, or failing to produce, or concealing, or attempting to conceal books, stocks, drugs or documents shall be guilty of an offence.

*Section 11*—Every regulation made under the Act is to be laid before Parliament.

*Section 12.*—The Secretary of State is empowered to grant licences or authorities on such terms and subject to such conditions, including the payment of a licence fee, as he thinks fit.

*Section 13*—Heavy fines with or without imprisonment for offences under the Act. If any person attempts to commit an offence, or solicits or incites another person to commit it, he shall, without prejudice to any other liability, be liable on summary conviction to the same punishment and forfeiture as if he had committed it. Where a person convicted of an offence is a company, the chairman and every director and every officer concerned in the management of the company shall be guilty of the like offence unless he proves that the act constituting the offence took place without his knowledge or consent.

*Section 14.*—Permits any constable to arrest without warrant in certain circumstances.

*Section 15*—Interpretation section, and includes the following definitions—

"**Raw Opium**" includes powdered or granulated opium, but does not include medicinal opium.

"**Prepared Opium**" means opium prepared for smoking, and includes dross and any other residues remaining after opium has been smoked.

"**Medicinal Opium**" means raw opium which has undergone the processes necessary to adapt it for medicinal use in accordance with the requirements of the *British Pharmacopœia*, whether it is in the form of powder or is granulated, or is in any other form, and whether it is or is not mixed with neutral substances

*Section 16.*—Application to Ireland

### **DANGEROUS DRUGS AND POISONS (AMENDMENT) ACT, 1923, SUMMARISED.**

(13 AND 14 GEO. V, CHAPTER 5.)

*This Act amends, by deletion, addition or substitution, certain of the sections of the Dangerous Drugs Act, 1920. The amendments have been incorporated in our notes on that Act. The only entirely new provision is contained in Section 5, which relates to the calculation of percentages in the case of liquid preparations, and, as amended by the Pharmacy and Poisons Act, 1933, is as follows:—*

*Section 5.*—For the purposes of Section 8 of the Dangerous Drugs Act, 1920, percentages, in the case of liquid preparations, shall, unless other provision in that behalf is made by regulations under those Acts respectively, be calculated on the basis that a preparation containing one per cent. of any substance means

†By an Order in Council, S.R. & O., 1933, No 800, these substances became drugs under Part III of the 1920 Act, but are not subject to the regulations which apply to the other drugs in that part. They are subject to special regulations, viz., The Methylmorphine and Ethylmorphine Regulations, 1933 (see page 1034).

a preparation in which one gramme of the substance, if a solid, or one millilitre of the substance, if a liquid, is contained in every one hundred millilitres of the preparation, and so in proportion for any greater or less percentage

### DANGEROUS DRUGS ACT, 1925, SUMMARISED

(15 AND 16 GEO V, CHAPTER 74)

*This Act amends, by deletion, addition or substitution, certain of the sections of the Dangerous Drugs Act, 1920, and the Dangerous Drugs and Poisons (Amendment) Act, 1923. The amendments have been incorporated in our notes on those Acts. The only entirely new provisions are contained in Sections 1 (ii) and 5, which respectively define "coca leaves" and "Indian hemp," and provide power to exclude certain preparations from Part III of the Dangerous Drugs Act, 1920, and are as follows —*

#### Section 1 Sub-section 2 —

**"Coca Leaves"** means the leaves of any plant of the genus *Erythroxylaceæ* from which cocaine can be extracted either directly or by chemical transformation.

**"Indian hemp"** means the dried flowering or fruiting tops of the pistillate plant known as *cannabis sativa* from which the resin has not been extracted, by whatever name such tops are called

Section 5 — If His Majesty in Council thinks fit to declare that a finding with respect to any preparation containing any of the drugs to which Part III of the Dangerous Drugs Act, 1920, as amended by this Act, applies, has in pursuance of Article 8 of the Geneva Convention been communicated by the Council of the League of Nations to the parties of the said Convention, the provisions of the said Part III shall as from such date as may be specified in the Declaration cease to apply to the preparation specified therein

### DANGEROUS DRUGS ACT, 1932, SUMMARISED.

(22 GEO V, CHAPTER 15)

*This Act amends, by deletion, addition or substitution, certain of the sections of the Dangerous Drugs Acts, 1920 to 1925. The amendments have been incorporated in our notes on those Acts*

*The only entirely new provisions are contained in Sections 2 and 4, which respectively provide for the prohibition of trade, etc., in new drugs, including power to apply Part III of the Dangerous Drugs Act, 1920 (described as the principal Act) with or without modifications to certain drugs, and provide power to alter or revoke Orders or Declarations in Council, and are as follows —*

Section 2 — (1) It shall not be lawful for any person in the United Kingdom to trade in or manufacture for the purpose of trade any products obtained from any of the phenanthrene alkaloids of opium or from the ecgonine alkaloids of the coca leaf, not being a product which was on the thirteenth day of July, nineteen hundred and thirty-one, being used for medical or scientific purposes

Provided that if His Majesty is at any time satisfied as respects any such product that it is of medical or scientific value, he may by Order in Council direct that this sub-section shall cease to apply to that product

If any person acts in contravention of this sub-section, he shall be guilty of an offence against the principal Act

(2) If it is made to appear to His Majesty that a decision with respect to any such product as is mentioned in sub-section (1) of this section has in pursuance of Article II of the Geneva Convention (No 2) been communicated by the Secretary-General of the League of Nations to the parties to the said Convention, His Majesty, by Order in Council, may, as the case requires, either declare that the provisions of the said Part III shall apply to that product in the same manner as they apply to the drugs mentioned in sub-section (1) of section eight of the principal Act as amended by this Act or apply the said Part III to that product with such modifications as may be specified in the Order.

(3) His Majesty may by Order in Council apply Part III of the principal Act, with such modifications as may be specified in the Order, to any of the following drugs, that is to say, methylmorphine (commonly known as codeine), ethylmorphine (commonly known as dionin) and their respective salts.

Section 4 — An Order or Declaration made by His Majesty in Council under the Dangerous Drugs Acts, 1920 to 1932, may be varied or revoked by a subsequent Order or Declaration made in the like manner and subject to the like provisions.

**DANGEROUS DRUGS (CONSOLIDATION) REGULATIONS, 1928 SUMMARISED.**

MADE UNDER SECTION 7 OF THE 1920 ACT FOR CONTROLLING THE MANUFACTURE, SALE, POSSESSION AND DISTRIBUTION OF DANGEROUS DRUGS 10 WHICH PART III OF THAT ACT APPLIES—S.R. & O. 1928, No. 981

*With the amendments of subsequent regulations (S.R. & O. 1932, No. 933, S.R. & O., Sept 13, 1933; S.R. & O. 1936) incorporated*

**REGULATION 1. Manufacture.**—Prohibited, except by an authorised person if (i) on authorised premises, and (u) in accord with the terms and conditions of his authority.

**2. Supply and procuring of drugs and preparations.**—Except as provided, a person shall not supply or procure, or offer to supply or procure, to or for any person (including himself), either in Great Britain or elsewhere, or advertise for sale, a drug, etc. (a) unless authorised, (b) otherwise than in accord with the terms and conditions of his authority, (c) if the drug, etc., is to be supplied to or procured for a person in the U.K., unless that person is authorised to be in possession, or to or for a person authorised, otherwise than in accord with the terms and conditions of that person's authority

In regard to (c), the administration of a drug, etc., by, or under the direct personal supervision, and in the presence of, a medical practitioner (or dentist for dental treatment) shall not be deemed supplying

**3. Possession.**—(1) A person shall not be in possession unless authorised (2) (a) A person to whom a drug, etc., is lawfully supplied on a prescription of a medical practitioner, dentist, or veterinary surgeon, or to whom a drug is lawfully supplied by a medical practitioner or veterinary surgeon, dispensing medicines, is authorised to be in possession

Provided that if a drug, etc., is supplied by, or on a prescription given by, a medical practitioner to a person who was at that time under treatment, whether for addiction or otherwise, from and being supplied with a drug, etc., by, or on a prescription given by, another medical practitioner, that person is not authorised to be in possession of the drug, etc., supplied by, or on the prescription given by, the first-mentioned medical practitioner if he did not, before the supply thereof to him, disclose that he was being treated and supplied by the other medical practitioner

(b) A person shall be deemed to be in possession if the drug is in his actual custody or is held by any other person subject to his control or for him or on his behalf

**4. Delivery to messengers.**—(1) Where a drug is to be lawfully supplied to anyone ("the recipient") otherwise than by, or on a prescription given by, a medical practitioner, the person supplying ("the supplier") shall not deliver it to a person who purports to be sent by or on behalf of the recipient unless that person (a) is an authorised person under the Acts, or (b) produces to the supplier a written statement signed by the recipient that he is authorised by the recipient to receive the drug on the latter's behalf, and the supplier is satisfied that the document is genuine. (2) A person to whom a drug is so delivered is an authorised person, but for such period only as reasonably suffices for the delivery

**5. General authority.**—(1) (a) Medical practitioners, (b) dentists, (c) veterinary surgeons, (d) pharmacists dispensing at a public hospital or institution, (e) persons in charge of a laboratory used for research or instruction and attached to an institution approved by the Secretary of State, (f) persons appointed by a local authority as analysts for the Sale of Food and Drugs Acts, 1875 to 1907, (g) inspectors appointed by the Pharmaceutical Society under the Pharmacy and Poisons Act, 1933 (added May 1, 1936, by Prov. S.R. & O. are authorised, so far as may be necessary for their professions or employments, as members of their respective classes, to be in the possession of and to supply the drugs, but a dentist may not supply drugs otherwise than by his personal administration to persons receiving treatment from him (2) An "institution" is a university, university college, public hospital, or other like institution

**6.** (1) Persons who are authorised sellers of poisons within the meaning of the Pharmacy and Poisons Act, 1933, are authorised (a) to manufacture on the registered premises in the ordinary course of their retail business (i) any extract or tincture of Indian hemp; (ii) any preparation; and (b) subject to the provisions of the Regulations, to carry on at the shop the business of retailing, dispensing or compounding drugs or preparations (amendments of Prov. S.R. & O. 1936,

incorporated in this sub-section). (2) Every drug or preparation in the actual custody of a person authorised by this Regulation shall be kept in a locked receptacle which can be opened only by him or by some assistant of his being a pharmacist.

**7. Withdrawal of authority.**—(1) If any authorised person is convicted of an offence against the Act, or under the Customs enactments as applied by the Act, the Secretary of State may, by notice in the *Gazette*, withdraw his authority, but, if he is authorised by virtue of the preceding Regulation, only after consulting the Council of the Pharmaceutical Society of Great Britain. (2) If the person whose authority is withdrawn is a medical practitioner, dentist, or veterinary surgeon, the Secretary of State may, by notice in like manner, direct that it shall be unlawful for that person to give prescriptions. (3) If the Secretary of State suspects that a medical practitioner or dentist is supplying or prescribing drugs to or for either himself or any other person otherwise than properly required for medical or dental treatment of himself or that other person, the Secretary of State may refer the matter to a tribunal constituted as stated in the First Schedule to these Regulations, and, if the tribunal so recommend, may, by notice in the *Gazette* withdraw the authority of the practitioner or dentist to supply, procure, or be in possession and direct that it shall be unlawful for him to give prescriptions.

**8.** (1) A prescription means a prescription directing the supply of a drug, and given either by a medical practitioner for medical treatment, by a dentist for dental treatment, or by a veterinary surgeon for animal treatment. (2) The prescription must (a) be in writing and be signed by the person giving it with his usual signature and be dated by him, and (b) except in a health insurance prescription, specify the address of the person giving it, (c) specify the name and address of the person for whose treatment it is given, or, if it is given by a veterinary surgeon, of the person to whom the article prescribed is to be delivered, (d) have written thereon, if given by a dentist, the words "For local dental treatment only," and, if given by a veterinary surgeon, the words "For animal treatment only," (e) specify, if it prescribes a preparation contained, or compounded of preparations all of which are contained, in the *B P*, the *B P C*, or the *N H I Drug Tariff*, the total amount of the preparation, or of each preparation, as the case may be, and in any other case the total amount of the drug to be supplied.

**9.** (1) A person shall not supply a drug on a prescription (a) unless the prescription complies with the above, and (b) unless in the case of a health insurance prescription he has no reason to suppose that it is not genuine, or, in the case of any other prescription, he either (i) is acquainted with the signature of the person by whom it purports to have been given, and has no reason to suppose that it is not genuine, or (ii) has taken reasonably sufficient steps to satisfy himself that it is genuine. (2) If a prescription expressly states that it may, subject to the lapse of a specified interval or intervals, be dispensed two or three times, the drug may be supplied a second or third time after the specified interval or intervals, but otherwise a prescription shall not be taken to authorise the drug to be supplied more than once. (3) The person dispensing shall, at the time, mark on the prescription the date on which it is dispensed, and, in the case of a prescription which may be dispensed two or three times, the dates of the second and third time, and, unless it is a health insurance prescription, retain it and keep it on the premises to be available for inspection.

**10. Marking of packages or bottles.**—(1) No person shall (a) supply a drug unless the package or bottle is marked with the amount contained, or (b) supply a preparation, unless the package or bottle is plainly marked (i) in the case of a powder, solution, or ointment, with the total amount contained and the percentage of the drug contained, or (ii) in the case of tablets or other similar articles, with the amount of the drug in each article and the number of articles contained. (2) This does not apply to a prescription lawfully given by a medical practitioner.

**11. Records.**—(1) Every person authorised to supply shall (a) keep a register and set out as in Parts I and II of the Second Schedule to these Regulations true particulars as to every quantity of drug or preparation obtained by him and supplied by him, whether to persons within or without Great Britain, (b) use a separate register or separate part of the register for each of the various classes of drugs and preparations, (c) make the entry on the day on which the drug is received, or on which the transaction takes place, or, if that is not practicable, on the following day, (d) keep a separate register in respect of each



set of business premises (subject to the approval of the Secretary of State, an authorised person may keep a separate register for each department of the business), (e) make no cancellation, obliteration, or alteration (any correction of an entry must be made by way of a marginal or foot note giving the date of correction), (f) on demand by the Secretary of State or by a person authorised in writing by him, furnish particulars required as to the obtaining or supplying or as to stocks, (g) the register may be used for entries required under Section 18 (2) (b) of the Pharmacy and Poisons Act, 1933 (amendment of Prov. S R. & O 1936 incorporated here), but, save as aforesaid, not for any other purpose (2) The entering in the register shall not apply to (a) a medical practitioner who enters in a day book particulars of every drug or preparation supplied by him to any person, with the name and address of that person, and the date of supply, and enters in a separate book kept for the purposes of the Regulation a reference to each entry in the day book which relates to the supply, or (b) an authorised seller of poisons within the meaning of the Pharmacy and Poisons Act, 1933 (amendment of Prov. S R. & O 1936, incorporated here) who enters in a separate book kept for the purposes of this Regulation a proper reference to each entry in a Pharmacy Act book which relates to the supply of any drug or preparation (3) References in the separate book must be made in chronological order, and the book must be kept in separate parts relating respectively to each of the several classes of drugs, and must not be used for any other purpose (4) The entry in the day book or separate book must be made on the day an entry would have been required to be made in the register (5) Every register, separate book, or day book in which any entry with respect to the supply of a drug or preparation is made, and every Pharmacy Act book containing an entry referred to in the separate book shall be kept on the premises to which the register or book relates or where the prescription was dispensed, so as to be available for inspection (6) Every entry and every correction must be made in ink, or indelibly written (7) In this Regulation (i) a drug or preparation administered by, or under the direct supervision and in the presence of a medical practitioner or a dentist, shall not be deemed to have been supplied by him, (ii) a "proper reference" means a reference entered in the separate book under the same date as the entry in the day book or Pharmacy Act book, and otherwise such as to enable the entry to be easily identified

**12. Export.**—(1) If any drugs or preparations authorised under the law of any country outside the U.K. to be exported therefrom to any destination outside the U.K. are brought into the U.K., no person shall without authority from the Secretary of State, cause or procure those drugs to be diverted to any other destination (2) The destination to which any drugs are authorised to be exported shall be taken to be that stated in the authority for export from the country of export

**13. Special provisions for ships.**—(1) The master of a ship not carrying a medical practitioner is authorised (a) so far as necessary for compliance with the Acts relating to merchant shipping, to be in possession of drugs and preparations, and (b) subject to conditions imposed by the Secretary of State, and Board of Trade instructions, to supply drugs to members of the crew (2) Where a drug is supplied to a member of the crew entry in the official log-book, in accordance with paragraph 5, Section 240, of the Merchant Shipping Act, 1894, of the treatment adopted shall be sufficient record, if the entry specifies the drug supplied (3) The master of a foreign ship in a port in Great Britain is authorised to purchase and be in possession of such quantity of drugs or preparations as may be certified by the M.O.H. of the port, or in his absence, the assistant M.O.H., to be necessary until the ship reaches its home port. A person who supplies a drug or preparation on such a certificate shall retain the certificate and mark it with the date the drug was supplied and keep it on his premises for inspection

**14.** All registers, records, books, prescriptions, and other documents kept, issued, or made in pursuance of the requirements of these Regulations must be kept, in the case of a register, book, or other like record, for two years from the date of the last entry, and in the case of any other document for two years from the date on which it is issued or made.

**15.** The Secretary of State may, subject to such conditions as he may prescribe, exempt any hospital or other public institution from any provision of these Regulations.

**16.** Nothing in these Regulations shall apply to any of the preparations mentioned in the Third Schedule to these Regulations, or to a drug or preparation denatured as approved by the Secretary of State.

17. (1) In these Regulations the following expressions have the meanings hereby assigned to them.

"Authority" means (a) any licence issued by the Secretary of State under Section 12 of the 1920 Act, (b) any authority granted by the Secretary of State under that Section and (c) any general authorisation; and the expression "Authorised" shall be construed accordingly.

"Drug" means any drug to which Part III of the 1920 Act applies, other than methylmorphine, ethylmorphine or their respective salts (amendment of S R. & O Sept 13, 1933, incorporated here), or a preparation within the meaning of these Regulations

"Preparation" means any preparation, admixture, extract or other substance containing such a proportion of a drug as is sufficient to make the preparation, admixture, extract or substance a drug to which Part III of the principal Act applies.

"Registered Premises" means premises duly registered under Part I of the Pharmacy and Poisons Act, 1933 (amendment of Prov. S R. & O 1936, incorporated here)

(2) For the purposes of these Regulations, but subject to any limitation attached to his authority (a) a person authorised to manufacture shall be deemed authorised to supply, and (b) a person authorised to supply shall be deemed to be a person authorised to be in possession of, to procure, to offer to supply or procure, and to advertise for sale

### FIRST SCHEDULE

*Constitution of Reference Tribunal for the purpose of Regulation 7, (3)*

Separate tribunals to deal respectively with persons practising in England and Scotland. Consisting, in the case of a medical practitioner, of three medical practitioners, and in the case of a dentist, of three dentists, together in either case with a legal assessor, the members of the tribunal and the legal assessor being appointed by the Secretary of State.

### SECOND SCHEDULE.

#### FORM OF REGISTER.

##### PART I—*Drugs or preparations obtained*

(The class of drugs and preparations to be specified at the head of each page)

Date on which received.	Name of person from whom obtained	Address	Amount obtained	Form in which obtained.
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##### PART II—*Drugs or preparations supplied*

(The class of drugs and preparations to be specified at the head of each page)

Date of transaction.	Name of person to whom supplied	Address	Authority of person to whom article supplied to be in possession thereof.	Amount supplied	Form in which supplied	In case of supply on a prescription, the ingredients of the prescription.
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## THIRD SCHEDULE

(as amended by S.R. &amp; O. 1932, No 933)

*Exempted preparations.*

- Cereoli Iodoformi et Morphinae, *B P C*  
 Emp. Opii, *B.P. '98*  
 Lin. Opii, *B.P. '14*.  
 Lin. Opii Ammon, *B.P.C.*  
 Pasta Arsenicalis, *B.P.C.*  
 Pil. Hydrarg. c. Opio, *B P C*  
 Pil. Ipecac. c. Scilla, *B.P. '14*  
 Pil. Plumbi c. Opio, *B.P. '14*  
 Pil. Digitalis et Opii Co., *B.P.C.*  
 Pil. Hydrarg. c. Cret. et Opii, *B P C*  
 Pulv. Cretæ Aromat. c. Opio, *B P. '32*.  
 Pulv. Ipecac. Co., *B.P. '14*.  
 Pulv. Ipecac. et Opii, *B.P. '32*  
 Pulv. Kino Co., *B.P. '14*  
 Suppos. Plumbi Co., *B P '14*  
 Suppos. Plumbi c. Opio, *B.P. '32*  
 Tablettæ Plumbi c. Opio, *B P.C.*  
 Ung. Gallæ c. Opio, *B.P. '14*  
 Ung. Gallæ Co., *B.P.C.*  
 Elixir Diamorphinae et Terpini c. Apomorphina, *B P C*.  
 Linctus Diamorphinae Camphoratus, *B P C*  
 Linctus Diamorphinae c. Ipecacuanha, *B P C*  
 Linctus Diamorphinae et Scillæ, *B.P.C.*  
 Linctus Diamorphinae et Thymi, *B P C*  
 Mixtures of Emp. Opii, *B.P. '98*, with other plasters of the *British Pharmacopœia* '14 and '32, and of the *British Pharmaceutical Codex*  
 Mixtures of Lin. Opii, *B.P. '14* with other liniments of the *British Pharmacopœia* '14 and '32, and of the *British Pharmaceutical Codex*  
 Mixtures of Lin. Opii Ammon, *B P C*, with other liniments of the *British Pharmacopœia* '14 and '32, and of the *British Pharmaceutical Codex*  
 Mixtures of Pulv. Ipecac. Co., *B.P. '14*, and of Pulv. Ipecac. et Opii, *B P '32*, with any of the following—  
     Hydrarg. c. Cret., *B.P. '14* and '32  
     Acetylsalicylic Acid.  
     Phenacetin  
     Quinine and its Salts  
     Sodium Bicarbonate  
 Mixtures of Ung. Gallæ c. Opii, *B P '14*, and of Ung. Gallæ Co., *B P C*, with other ointments and plasters of the *British Pharmacopœia* '14 and '32, and of the *British Pharmaceutical Codex*  
*Note.*—Although exempt from the provisions of the Dangerous Drugs Acts and Regulations, these preparations are subject to the provisions of the Pharmacy and Poisons Acts and of the Rules made thereunder.

### DANGEROUS DRUGS (HOSPITAL GENERAL EXEMPTION) ORDER (1924), SUMMARISED

By Order dated August 9, 1924, certain hospitals and other institutions are exempted from operation of the Regulations on compliance with certain conditions. This Order substitutes and revokes an Order on the same subject made August 15, 1921. Exempted are:—Any hospital or infirmary, asylum, poor-law institution or sanatorium supported by any public authority, or out of public funds or by a charity or voluntary subscription, in which the drugs are dispensed by a medical practitioner or a pharmacist or—in a poor-law institution—a dispenser whose qualifications and appointment are approved by the Minister of Health, if the conditions of Schedule I (below) are complied with, or, if there is no such dispenser, if the conditions of Schedule II (below) are complied with. Any institution exempted under this Order may be inspected at any time by any person so authorised by the Secretary of State, to ensure that the prescribed conditions are being fulfilled.

## SCHEDULE I.

- 1 Orders for supplies must be signed by the pharmacist, or if no such person is employed, by one of the medical practitioners attached to the hospital.
- 2 Supplies to be kept in the charge of the person responsible for dispensing, and records to be kept.
- 3 The medicine only to be dispensed for use of an individual patient, etc.
- 4 The person responsible for dispensing the drugs shall at the time of dispensing any prescription stamp, or otherwise mark, the prescription with the prescribed particulars, and shall keep records.
- 5 Prescriptions must be kept for two years.
- 6 Stock preparations in wards or out-patient department shall only be supplied on the requisition of the sister in charge, who shall keep the drugs under lock and key, and only be used by her in accordance with the directions of one of the medical practitioners in charge of the patients.
- 7 A requisition shall be marked in the dispensary to show that it has been complied with, filed there, and a copy or note of the requisition kept by the sister in charge.
- 8 Precautions shall be taken to prevent any theft of the drugs.
- 9 Preparations may be prescribed by any name known in the hospital.
- 10 Nothing in this Schedule shall affect any medicine or other substance to which the Regulations do not apply.

## SCHEDULE II.

Supplies are to be to, or on the order of, a medical practitioner attached to the hospital (not the dispenser), and he must certify that the supply is necessary for the treatment of the patients. The matron is to be responsible for keeping the drugs (in a locked cupboard, of which she alone shall have the key), and for using or administering them and recording their purchase, but they are only to be used, etc., under the direction of a medical practitioner attached to the hospital. Except so far as this Schedule modifies them, the Regulations must be observed—for instance, the chemist supplying a hospital must record the supplies get them signed for and mark the packages as on ordinary sales.

## NURSING HOMES.

The Dangerous Drugs (Hospital General Exemption) Order (1924) does not apply to nursing homes, and drugs to which the Dangerous Drugs Acts and Regulations apply may only be supplied for the use of patients in like manner as the drugs may be supplied to patients in their own homes. A separate prescription must be written by the medical practitioner for the individual patient. The nursing home may not hold a "stock" of drugs. For a note of the conditions under which poisons other than "dangerous drugs" may be supplied to nursing homes to hold as a "stock," see page 990.

## SPECIAL AUTHORISATIONS.

Although persons within the classes indicated below may be supplied with the preparations mentioned, they must comply with the special conditions laid down for each by the Home Office.

In supplying the drugs to the authorised persons the full requirements of the Dangerous Drugs Acts and Regulations, and of the Pharmacy and Poisons Act and Rules, must be observed.

**Laudanum to Farmers and Stock-owners.** (Aug 1921.)

Tincture of opium may be sold to farmers and stock-owners if they have been granted by the Chief Officer of Police for the area in which they carry on business an authority to obtain tincture of opium to be used solely for the treatment of animals. The drug must be obtained from the person specified in the Authority. Not more than 32 fluid ounces may be supplied on each Authority.

**Cocaine in Castor Oil to Factory Occupiers.** (Aug. 1921.)

Eye-drops, consisting of not more than 1 part of cocaine in 200 of castor oil, with not less than 1 part in 3000 of mercuric chloride, may be sold to the occupier of a factory or workshop to which the Factory and Workshops Act, 1901, applies.

**Preparations Containing Opium to Midwives.** (Aug 1921.)

Preparations containing opium (but not morphine tablets) may be sold to certified and practising midwives so far as is necessary for their midwifery practice.

**Cocaine in Castor Oil to Owners of British Steam Fishing Vessels.**  
(Dec 1927.)

Eye-drops of the same formula as that indicated for supply to factory owners may be sold to the owner of a British steam fishing vessel. For conditions of authority of masters of British or foreign ships (other than British steam fishing vessels) to be in possession of certain drugs, see Regulation 13 of the Dangerous Drugs (Consolidation) Regulations, 1928, page 1028

**Agents of Overseas Governments.** (Dec 1933)

Certain persons named in the Schedule to the authorisation may procure "dangerous drugs" for their respective governments. The drugs must be obtained from persons or firms licensed to supply them. The persons named are *not* authorised to be in possession of the drugs

**RAW OPIUM REGULATIONS SUMMARISED.**

MADE UNDER SECTION 3 OF THE 1920 ACT FOR CONTROLLING AND RESTRICTING THE POSSESSION, SALE AND DISTRIBUTION OF RAW OPIUM—S R & O 1921, No. 864.

*With the amendments of subsequent regulations (S R & O 1922, No. 1086, S R. & O. 1923, No. 311, S R & O 1924, No. 1292, Prov S R & O, May 1, 1936) incorporated*

**1. Sale and Distribution.**—No person shall supply or procure, or offer to supply or procure raw opium to or for any person, whether in the United Kingdom or elsewhere, or shall advertise raw opium for sale—(a) unless licensed or authorised (amendment of S R & O 1923, No. 311, incorporated here); or (b) otherwise than in accord with the terms and conditions of the licence or authority

**2.** No person shall supply or procure, or offer to supply or procure, raw opium to or for any person who is not licensed or authorised to be in possession of it, and then only in accord with the terms and conditions of the licence or authority of that person.

**3. Possession.**—No person shall be in possession, or attempt to obtain possession of, raw opium (amendment of S. R. & O 1922, No. 1086, incorporated here) unless (a) licensed to import or export, or (b) licensed or authorised to supply, or (c) otherwise licensed or authorised to be in possession of it

**4. Records.**—A person who supplies raw opium shall (a) enter in a register kept for the sole purpose all supplies purchased or obtained, and all dealings effected (including sales or supplies to persons outside the United Kingdom) as shown in the Schedule to these Regulations; (b) make entry with respect to purchases on the day it is received and with respect to sales or supplies by him on the day on which the transaction is effected, or if not reasonably convenient on the day following; (c) if he carries on business at more than one address, keep a separate register for each set of premises, (d) keep the register on the premises to which it relates and available for inspection, (e) not cancel, obliterate or alter any entry or make any untrue entry. Any mistake in an entry may be corrected by a marginal note or footnote giving the correct particulars, and dated

The forms of records are as follows:—

(a) *Record of Raw Opium purchased or otherwise obtained.*

Date on which supply received.	Name of person, body or firm from whom obtained	Address of person, body or firm from whom obtained.	Amount obtained.	Form in which obtained, i.e., raw, powdered or granulated.

*(b) Record of Raw Opium sold or supplied.*

Date on which the transaction was effected	Name of person, body or firm to whom sold or supplied	Address of person, body or firm to whom sold or supplied.	Authority of person, body or firm to be in possession of raw opium	Amount sold or supplied	Form in which sold or supplied, i.e., raw, powdered or granulated

The registers are to be kept two years from date of last entry (S R & O. 1922, No 1086)

**5. General Authorisations.**—Any duly qualified medical practitioner, or any authorised seller of poisons within the meaning of the Pharmacy and Poisons Act, 1933, or any person employed or engaged in dispensing medicines at any public hospital or other public institution, being a person registered under the Pharmacy and Poisons Act, 1933, or any registered veterinary surgeon, or any person in charge of a laboratory for purposes of research or instruction attached to any university, university college, public hospital or other institution approved by the Secretary of State for the purpose, or any person appointed by a local authority with the approval of the Minister of Health as an analyst for the purposes of the Sale of Food and Drugs Acts, 1875 to 1907, is authorised so far as is necessary for the practice of his profession or employment in such capacity to be in possession of and supply raw opium, but subject always to the keeping of records as required by Regulation 4 above

6. In certain circumstances authorisations under the preceding Regulation may be withdrawn by the Secretary of State

**7. Delivery to Messengers.**—Delivery shall not be made to a person not licensed or authorised to be in possession who purports to be sent by or on behalf of a licensed or authorised person unless he produces an authority in writing, signed by the person licensed or authorised to receive it on his behalf, and unless the person supplying is satisfied that the authority is genuine (In the case of raw opium there is no exemption for prescriptions)

**8. "Possession."**—Raw opium in the order or disposition of anyone is in his possession

**9. Application to Ireland.**—As under Section 16 (a) of the 1920 Act, *q v*

**10. Diversion in Transit.**—If any consignment of raw opium to some destination outside the United Kingdom is brought into any port in the United Kingdom no person shall, unless specially licensed, divert it, or cause or procure it to be diverted, to any destination other than that to which it was originally consigned, namely, the destination stated in the licence or other authority to export it granted by the Government of the country of export (amendment of S R & O 1924, No 1292, incorporated here)

**11.** Future copies of these Regulations, printed by H M Stationery Office, may include any amendments, and the Regulations as amended may be called the Raw Opium Regulations (amendment of S R & O 1923, No. 311, incorporated here)

### COCA LEAVES AND INDIAN HEMP REGULATIONS SUMMARISED.

MADE UNDER SECTION 3 OF THE 1920 ACT, FOR CONTROLLING AND RESTRICTING THE POSSESSION, SALE AND DISTRIBUTION OF COCA LEAVES AND INDIAN HEMP — S.R. & O. 1928, No. 982.

1 Subject to these Regulations, the Raw Opium Regulations apply to (a) coca leaves, (b) Indian hemp and resins obtained from Indian hemp, and all preparations (except extract and tincture of Indian hemp) of which such resins form the base.

2 (i) Separate registers or separate parts of the register used for raw opium shall be used for (a) coca leaves and (b) Indian hemp. (ii) The form of the registers shall be as for raw opium but with the words "raw, powdered or granulated" omitted.

### METHYLMORPHINE AND ETHYLMORPHINE REGULATIONS SUMMARISED.

MADE UNDER SECTION 7 OF THE 1920 ACT, AND SECTION 2 (3) OF THE DANGEROUS DRUGS ACT, 1932, FOR CONTROLLING THE MANUFACTURE, SALE, POSSESSION AND DISTRIBUTION OF METHYLMORPHINE (COMMONLY KNOWN AS CODEINE), ETHYLMORPHINE (COMMONLY KNOWN AS DIONIN) AND THEIR RESPECTIVE SALTS.—S.R. & O, Sept 13, 1933

**REGULATION 1. Manufacture.**—Prohibited, except by a licensed person and in accord with the terms and conditions of his licence

**2. Supply of drugs.**—Except as provided, a wholesale druggist shall not supply a drug to any person either in Great Britain or elsewhere (a) unless licensed, (b) otherwise than in accord with the terms and conditions of his licence, (c) if the drug is to be supplied in any one transaction in quantity exceeding one pound avoirdupois, unless the person to whom it is to be supplied is licensed to be in possession of the drug.

**3. Possession.**—(1) A person shall not be in possession of a drug in a quantity exceeding one pound avoirdupois unless he is so licensed

(2) A person shall be deemed to be in possession if the drug is in his actual custody, or is held by any other person subject to his control or for him or on his behalf.

**4. Marking of packages or bottles.**—No wholesale druggist licensed to supply a drug shall supply it unless the container is plainly marked with the amount of the drug contained therein

**5. Keeping of registers.**—Every wholesale druggist licensed to supply shall (a) keep a register, and set out as in the Schedule to these Regulations true particulars as to every quantity of drug obtained by him and supplied by him, whether to persons within or without Great Britain, (b) use a separate register or separate part of the register for (i) methyilmorphine and its salts, (ii) ethyilmorphine and its salts, (c) make the entry on the day on which the drug is received or on which the transaction takes place, or, if that is not practicable, on the following day, (d) keep a separate register in respect of each set of business premises (subject to the approval of the Secretary of State, a licensed wholesale druggist may keep a separate register for each department of the business), (e) make no cancellation, obliteration, or alteration (any correction of an entry must be made by way of a marginal or foot note, giving the date of correction), (f) on demand by the Secretary of State, or by a person authorised in writing by him, furnish particulars as to the obtaining or supplying, or as to stocks, (g) the register may be used for entries required under the Pharmacy and Poisons Acts, 1852-1933, but, save as aforesaid, not for any other purpose, (h) every register shall be kept on the premises to which it relates, and so as to be at all times available for inspection

**6. Preservation of registers.**—All registers which are kept in pursuance of the requirements of these Regulations are to be kept for a period of two years from the date of the last entry

**7. Regulations not to apply to certain types of sale.**—Nothing in these Regulations shall apply to any sale or distribution of any of the drugs by a person other than a wholesale druggist, nor to any sale or distribution by an authorised seller of poisons in the course of any retail business.

**8. Interpretation.**—(1) In these Regulations the following expressions have the meanings hereby assigned to them—

"Licence" means any licence issued by the Secretary of State under Section 12 of the Dangerous Drugs Act, 1920, and the expression "licensed" shall be construed accordingly.

"Authorised seller of poisons" means a person lawfully carrying on business in accordance with the provisions of the Pharmacy and Poisons Act, 1933, as an authorised seller of poisons

"Drug" means Methyilmorphine, Ethyilmorphine and their respective salts

"Retail business" means the business of retailing or dispensing (or compounding) drugs carried on at a shop.

"Wholesale druggist" means a person who carries on the business of selling drugs to persons who buy to sell again.

(2) For the purpose of these Regulations, but subject to any limitation attached to his licence: (a) a wholesale druggist licensed to manufacture a drug shall be deemed licensed to supply; and (b) a wholesale druggist licensed to supply shall be deemed to be a person licensed to be in possession of that drug for the purpose of Regulation 3 of these Regulations.

SCHEDULE  
FORM OF REGISTER  
PART I.—*Drugs obtained*

(The class of drugs to which the entries relate to be specified at the head of each page in the Register)

Date on which received	Name	Address	Amount obtained	Form in which obtained
	of person from whom obtained			

PART II —*Drugs supplied*

(The class of drugs to which the entries relate to be specified at the head of each page in the Register.)

Date of transaction	Name	Address	*Description.	Amount supplied	Form in which supplied
	of person to whom supplied				

\**i.e.*, wholesale druggist, medical practitioner, pharmacist, etc

**THERAPEUTIC SUBSTANCES ACT, 1925, SUMMARISED.**

(15 AND 16 GEO V, CHAPTER 60)

AN ACT TO PROVIDE FOR THE REGULATION OF THE MANUFACTURE, SALE, AND IMPORTATION OF VACCINES, SERA, AND OTHER THERAPEUTIC SUBSTANCES.

**1** This Act applies to —

- (1) Vaccines, sera, toxins, antitoxins and antigens
  - (2) Salvarsan (dioxo-diamino-arseno-benzol-di-hydrochloride) and analogous substances used for the specific treatment of infective diseases
  - (3) Preparations of the specific antidiabetic principle of the pancreas known as insulin
  - (4) Preparations of the posterior lobe of the pituitary body intended for use by injection
  - (5) Sterilised surgical ligature and sterilised surgical suture (*i.e.*, any ligature or form of binding material prepared from the gut or any tissue of an animal, and offered or intended to be offered for sale as sterile and ready for use in surgical operations upon the human body) (Added S.R. & O. 1931, No. 633.)
- and any other therapeutic substances, afterwards called "substance," which may from time to time be added by regulations made under this Act as being substances the purity or potency of which cannot be adequately tested by chemical means.

- 2.** (1) To manufacture for sale any substance to which this Act applies licences (personal and premises) from the licensing authority are required.
- (2) The licence continues in force for such period as may be prescribed (two years), but may from time to time be renewed for a like period.



- (3) The conditions under which the substances are manufactured, and the premises, must satisfy the licensing authority.
- (4) A licence may be revoked or suspended if the licensee fails to comply with the requirements.
- (5) This section does not apply to the preparation by a medical practitioner for any of his own patients or for, and at the request of, another practitioner, if specially prepared with reference to the condition, and for the use, of an individual patient.
3. (1) Importation into Great Britain or Northern Ireland necessitates standards of strength, quality and purity, and the substance is to be consigned to a person licensed by the licensing authority to import, or to a person engaged in scientific research holding a special licence to import.
- (3) Substances prohibited come under Section 42 of the Customs Consolidation Act, 1876, and any Act amending or extending
4. (1) Joint Advisory Committees frame regulations
5. (1) The joint committee has power to make regulations for prescribing standards, tests, adding to the Schedule, prescribing the forms of licences, including inspection of premises and plant, and to take samples, and to exclude any substance used solely for veterinary purposes. If advertised or sold as a proprietary medicine or contained in such medicine, such accepted scientific name, or name descriptive of the true nature and origin of the substance, as may be prescribed, shall appear on the label. Date of manufacture shall be stated on all vessels or packages, and the sale is prohibited after the expiry of the prescribed period.
6. Contravention of the Act renders a person liable on summary conviction to a fine not exceeding £100, and on second or subsequent convictions to a fine and imprisonment, with or without hard labour for not exceeding three months, and in either case goods to be forfeited and licence may be revoked or suspended.
7. (1) The licensing authorities are for England and Wales, the Minister of Health, for Scotland, the Scottish Board of Health, for Northern Ireland, the Minister of Home Affairs for Northern Ireland.

### THERAPEUTIC SUBSTANCES REGULATIONS, 1931, SUMMARISED.

**PART I. Interpretation; revocation of Regulations; addition of sterilised surgical ligature and suture as substances to which the Act of 1925 applies; licences and applications for licences.**

**PART II. Licences for manufacture of therapeutic substances.**

6. Applicant to satisfy the licensing authority that upon issue or renewal of licence the conditions set out in No. 7 of these Regulations will be observed
7. (a) Concerns provision of adequate staff and premises for manufacture  
 (b) And for tests of the strength, quality and purity of the substance, including housing for animals used, the licensee shall maintain staff and premises to carry out tests, or make arrangements with some institution approved for such tests to be regularly carried out on his behalf  
 (c) Records of manufacture and tests to be kept with batch-number  
 (d) Inspectors may inspect the premises and plant, and the process of manufacture and the means employed for standardising and testing, and may take samples.  
 (e) Any changes in the expert staff responsible and in the premises or plant to be reported  
 (f) Samples to be furnished on request  
 (g and h) Batches may be withheld from sale  
 (i) Licensee to comply with Parts III and IV and further requirements if necessary.

**PART III. Provisions with regard to names of substances and to containers, etc.**

8. *Name of Substance.*—If any substance is advertised or sold as a proprietary medicine, or is contained in a medicine the "proper name" of the

substance shall appear on the label in the manner prescribed in this Part of these Regulations

9. **Containers.**—The substance is to be sealed in a previously sterilised glass container (Ligatures and sutures may be in containers other than glass.)
10. **Labelling**—The following are required on every sealed container —
  - (a) The proper name of the substance in letters not less conspicuous than those in which the proprietary name, if any, is written or printed, and following immediately after or under such proprietary name
  - (b) The number of the licence under which the substance is manufactured preceded, in the case of import licences, by the words "Import Licence."
  - (c) A distinctive batch-number
  - (d) Where a test for potency in units is required by these Regulations, a statement of the potency in units defined in terms of relation to the standard preparation described under these Regulations (This does not apply to vaccine lymph or sterilised surgical ligature or suture)

In addition to the above, the following particulars together with any others specified in the relative schedule must appear either on the label on the container or on a label or wrapper affixed to any package in which the container is issued for sale —

  - (e) The name and address of the maker, date of manufacture, and statements of toxicity if required, nature of antiseptic if any, are also enforced, also date of removal from cold storage at a temperature not exceeding 5°C
11. The sale of a substance after prescribed date is prohibited, but a doctor may override this, if his attention has been drawn to the date and he is satisfied it is required by the urgency of the case

#### **PART IV. Standards of strength, quality and purity, and tests for determining.**

15. Tests for living aerobic or anaerobic bacteria are to be made in the case of —
  - (a) Sera and solutions of serum proteins for injection
  - (b) Certain bacterial vaccines (anti-typhoid, anti-typhoid-paratyphoid (T A B), anti-typhoid-paratyphoid-cholera (T A B C), anti-plague, anti-dysentery, and whooping-cough vaccines).
  - (c) Toxins, antigens, and mixtures of toxins or antigens with serum which are intended to be used in medical practice for immunising treatment, or for diagnosis by inoculation of the patient.
  - (d) Solutions of insulin
  - (e) Dry preparations of insulin intended for therapeutic use
  - (f) Preparations of the posterior lobe of the pituitary body intended for use by injection, except preparations which, after being sealed in the containers, have been sterilised by heat in a manner satisfactory to the licensing authority
16. The tests are to be applied —
  - (a) To samples taken from each batch of the substance before filling and sealing the containers, and
  - (b) To the contents of sample containers when ready for issue
17. (a) In the case of samples taken from the batch at the time when the test is made, the quantity taken for test shall be not less than 0.1% of the total volume of the batch if the volume is not more than 10 litres, and not less than 10 Cc. if the volume is 10 litres or more, but shall in no case be less than 1 Cc. If the batch is contained in a number of bulk containers, samples in these proportions shall be taken from each of such bulk containers and separately tested.
- (b) In the case of the contents of sample containers, the number shall be not less than 1% of the total filled from the batch, if this number is not more than 1,000, and not less than 10 if the total number is more than 1,000
18. Defines method of preparing and using media.
19. (1) In the case of samples taken from the batch, one-half of the total volume of the sample is to be used for aerobic and one-half for the anaerobic test.

- (2) In the case of the contents of sample containers, the contents of each container shall be tested for aerobic and anaerobic organisms. When the volume in each container is 2 Cc. or more, 1 Cc. shall be used for each test. When the volume in the container is less than 2 Cc., the contents shall be divided into two approximately equal parts, one for the aerobic and the other for the anaerobic test.
- (3) The inoculated tubes shall be incubated at 37°C. for five days and examined after incubation, permanent records being kept of such examination of each tube.
20. (1) If at this examination no growth is found in any tube, the sample has passed the test.
- (2) If at the examination a growth is visible, further samples may be taken and the tests repeated. The taking of samples from the batch may, if necessary, be repeated twice. If the same organism is visible in more than one test, the batch shall be treated as not sterile, and the material contained in the batch shall not be issued or used as part of a further batch unless and until it has been re-sterilised and has passed the tests.
21. Emergency Regulations
22. Freedom from abnormal toxicity is ensured by injecting 0.5 Cc. of the serum into a normal mouse, and 5 Cc. into a normal guinea-pig.

#### **PART V. Licences for import of substances.**

- 23 and 24.—Broadly, the applicant must furnish a written undertaking signed by, or on behalf of, the manufacturer that the manufacturer will comply with the Regulations as to manufacture and testing.

#### **PART VI. 25. Research Licences.** Special modifications apply

- PART VII. 26. Substances manufactured or imported for export only.**  
The licensing authorities may dispense with any of the requirements of the Regulations, if necessary.

#### **PART VIII. Substances for veterinary use only.**

27. Containers to be marked "to be used solely for veterinary purposes"  
In respect of ligatures and sutures, the labelling of wrapper affixed to package in which the container is issued, suffices.

**FIRST SCHEDULE** provides forms of application for, and grant of, licences

#### **SECOND SCHEDULE, PART I. Vaccines, toxins, antigens, sera and antitoxins.**

- (A) Provisions applicable to the production of bacterial vaccines

- (1) Defines a bacterial vaccine
- (2) Requirements in respect of the staff of manufacturer
- (3) The proper name of a vaccine is the name of the micro-organism followed by the word "vaccine," except in the following —  
Anti-typhoid vaccine, anti-typhoid-paratyphoid vaccine (T A B), anti-typhoid-paratyphoid-cholera vaccine (T A B C), anti-plague vaccine, whooping-cough vaccine, anti-dysentery vaccine
- (6) The label on the container must indicate composition —
  - (a) Number of micro-organisms per Cc. or
  - (b) Weight of dried substance of micro-organisms per Cc. or
  - (c) Number of micro-organisms or weight of dried substance of organisms used in preparing 1 Cc. of the finished product

- (B) Special provisions for Vaccine Lymph (Vaccinia).

- (1) The proper name is "Vaccine Lymph."

Staff of establishment, housing of animals, precautions to observe, containers, labelling, tests for purity (glycerination and cold storage, tests of gas-producing anaerobic organisms, living hæmolytic streptococci) and potency are included

#### **PART II. Toxins and antigens.**

- (A) Provisions applicable to reagents used in the Schick Test for the diagnosis of susceptibility to diphtheria

- 1.—(1) The reagents used in the Schick Test are two, Schick Toxin and Schick Control. Their proper names respectively are "Schick Test Toxin" and "Schick Control"
- (2) Schick Toxin is a sterile filtrate from a culture on nutrient broth of the specific organism of diphtheria (*Corynebacterium diphtheriæ*). It may be issued either (i) undiluted, or (ii) already diluted with saline solution to the strength proper for use in the test

- (3) Schick Control is prepared from the same batch of Schick Toxin as that with which it is issued for sale, by destroying the specific toxicity at 70°C. for a time not shorter than 5 minutes
2. Tests for potency.
- (B) Provisions for Diphtheria Prophylactic (amended by S R & O. 1935, No 580)
- (C) Provisions for Tuberculins and other preparations from the bacillus tuberculosis and its cultures

**PART III.** Provisions applicable to production of all sera from living animals.

**PART IV.** Provisions for particular sera and antitoxins

- (A) Anti-bacterial sera and anti-toxic sera for which no potency test is prescribed.
- (B) Anti-dysentery serum (Shuga) and other anti-dysentery sera.
- (C) Diphtheria antitoxin.
- (D) Tetanus antitoxin.
- (E) Gas-gangrene antitoxin (*perfringens*).
- The following have been added by S R. & O. 1935, No. 580 —
- (F) Antipneumococcus serum (Type I)
- (G) Antipneumococcus serum (Type II).
- (H) Staphylococcus antitoxin
- (I) Gas-gangrene antitoxin (*oedematiens*).
- (J) Gas-gangrene antitoxin (*vibrion septique*).

**THIRD SCHEDULE. Arsphenamine and derivatives.**

**PART I.** General provisions applicable to arsphenamine and derivatives.  
The standard preparations are kept in the National Institute for Medical Research, Hampstead. Biological tests are applied and tests for maximum toxicity and for therapeutic potency

**PART II.** Special provisions for arsphenamine Chemical and physical.

**PART III.** Special provisions for neo-arsphenamine

**PART IV.** Special provisions for sulpharsphenamine.

**PART V.** Special provisions for derivatives of arsphenamine other than neo-arsphenamine and sulpharsphenamine

**FOURTH SCHEDULE. Insulin.**—Proper name Special conditions of licence Standard. Units Quality Tests. Container Label

**FIFTH SCHEDULE. Pituitary (Posterior Lobe) Extract.**—Proper name. Standard Units Quality. Tests Container Label

**SIXTH SCHEDULE. Sterilised Surgical Ligature and Suture.**—Proper name. Tests for sterility Label

## THERAPEUTIC INDEX OF DISEASES AND SYMPTOMS

This index is included as a general guide to treatment by drugs and is intended to refer the reader to the text, where a full account is given of the uses of each drug in the index.

*For bacteriological and clinical notes with reference to special diseases, see 20th Edition, Vol II, p 509, et seq*

**Abortion, Threatened.**—Hydrastis, Ovarian Hormones, Quinina (and Salts), Sumbul, Viburnum

**Abrasions and Cuts.**—Acriflavina, Collod Aceton, Collod Stypt., Iodum, Lint Acid. Boric., Liq Hamam, Mercurochromum, Tinct Benzoin Co

**Abscesses, Dental.** *Local*—Emplastrum Capsici Mitis *vel* Fortis, Iodum, Liq Iod Mit, Lot Acid Boric

**Abscesses, General, to abort.**—Aconitum, Belladonna, Calx Sulphurata, Mangani Butyras, Quinidina, Quinina, Vaccinum Staphylococcicum

*Local*—Argenti Nitras, Past Bism et Iodof, Phenol, Liq Calc Chlorinat c Acid Boric, Liquor Hydrogenii Peroxidi Liq Iod Mit, Liq Sod Chlorinat Chur, Ung Bellad, Ung Iod Denig

**Abscess, Liver, Tropical.**—Antimonial, Arsenicals, Auremetine, Emetine injections, Ipecacuanha, Quinine injections, Vaccine of organism if isolated

**Absorbents.** (*Toxins*)—Carbo, Creta, Kaolinum, Magnesii Trisilicas (*Gaseous Products*)—Carbo (*Alkaloidal Poisons*)—Carbo, Kaolinum

*Local (Protective)*—Amylum, Bismuthi Subchloridum, Talcum Purificatum, Zinci Oxidum

**Achlorhydria.**—Acidum Hydrochloricum, Betainæ Hydrochloridum, Gentiana, Nux Vomica

**Acidity of Stomach.**—*See* Antacids.

**Acne.**—Arseni Trioxidum, Calci Chloridum, Calx Sulphurata, Cerevisiæ Fermentum, Ferri Cacodylas, Oleum Morrhuæ, Phosphorus, Potassii Bromidum, Sodii Bromidum, Stanni Oxidum, Sulphur, Vaccinum Staphylococcicum (subcutaneous)

*Local*—Acidum Salicylicum, Calamina, Chrysarobinum, Ichthammol, Phenol, Resorcinol, Sulphur Sublimatum, Sulphuris Iodidum, Thymol, X-Rays.

**Actinomycosis.**—Cupri Sulphas, Inj Sol Argent Nit 20%, Iodine Injections, Potassii Iodidum; Salicylates, Sodii Iodidum, Vaccin Actino

*Local*—Argent Colloid, Cupri Sulphas, X-Rays

**Addison's Disease.**—Arseni Trioxidum, Extractum Suprarenali Corticis, Ferrum, Phosphorus, Sodii Chloridum

**Adenoids.**—Ferrum, Iodum, Liq Ferr Pepton c Mang, Oleum Morrhuæ, Syr Iodo-Tannic

*Local*—Ammonii Chloridum, Glycer Ferr Perchlor, Neb Acid Tannic, Pasta Londinensis, X-Rays

**Adhesions, Fibrous, Peritoneal, etc.**—Inj Thiosinam et Phenazon, Inj Thiosinam et Sod Salicyl

**Adiposity.**—*See* Obesity.

**Ague.**—*See* Malaria.

**Albuminuria.**—Acidum Gallicum, Ferri Cacodylas, Liq Ferr et Ammon Acet, Liquor Glycyllis Trinitratis, Oleum Juniperi, Vin Diuret, Viscum

**Albuminuria, Functional.**—Calci Chloridum, Calci Lactas, Magnesii Carbonas.

**Alcoholism.**—*See* Dipsomania.

**Alopecia.**—Arseni Trioxidum, Hæmoglobinum, Iron Salts, Pilocarpina, Thyroideum

*Local*—Liq Ammon Dil; Cantharidinum; Cantharis, Capsicum, Hydrargyri Oxidum Rubrum, Jaborandi, Mylabris; Oleum Myristicæ, Oleum Rosmarini, Resorcinol

**Amenorrhœa.**—Aloe; Aloinum, Apioi, Calendula, Caulophyllum, Ergota, Gossypii Cortex; Helleborus Niger, Iron Salts, Mangani Dioxidum, Mist Ferri Co.; Oleum Hedeomæ, Oleum Juniperi, Oleum Petroselinii, Oleum Pulegii; Oleum Rutæ, Oleum Sabinæ; Ovarian Hormones; Potassii Permanganas, Pulsatilla; Ruta; Sabina.

*Local.*—Mustard Sitz-bath.

**Amœbiæ.**—Acetarsol, Auremetine; Carbarsone, Chiniofonum, Emetina, Emetinæ Periodidum, Emetinæ et Bismuthi Iodidum, Ipecacuanha

**Anæmia.**—Acidum Cacodylicum (and Salts), Arseni Trioxidum, Cupri Sulphas, Ferri Albuminas, Ferri Arsenas, Ferri Carbonas, Ferri et Ammonii Citras, Ferri et Ammonii Citro-Arsenis, Ferri Glycerophosphas, Ferri Peptonas, Ferri Perchloridum, Ferri Phosphas Saccharatus, Ferri Sulphas, Ferrum Redactum, Hæmoglobinum, Manganese Salts, Medulla Rubra, Mist Ferri Aperiens, Mist Ferri Co, Pil Aloes et Ferr, Pil Aloes et Myrrh, Pil Ferr et Arsen, Pil Ferri Carb., Sodii Aminarsonas, Sodii Arsenas Anhydrosus, Syr Ferr Bromid

**Anæmia, Pernicious.**—Acidum Hydrochloricum, Anahæmin, Extractum Hepatis Liquidum and Siccum, Ventriculus Desiccatus

**Anæsthetics.** *General*—Acetylene, Æther Anæstheticus, Æthylum, Æthylis Chloridum, A C E; Avertin, Chloroformum, Cyclopropane, Nitrogenii Monoxidum; Vinyl Ether *Local*—Æthylis Bromidum, Æthylis Chloridum, Amydricainæ Hydrochloridum, Amylocainæ Hydrochloridum, Benzaminæ Hydrochloridum, Benzaminæ Lactas, Benzocaina, Cocaina, Orthocaina, Phenacainæ Hydrochloridum, Procainæ Hydrochloridum, Quininæ et Ureæ Hydrochloridum *Spinal*—Amylocainæ Hydrochloridum, Procainæ Hydrochloridum *Surface*—Cocaina (and Salts)

**Anæsthetics, Hypnotics to use with**—Alcohol Tribromethylis, Barbiturates, Morphina, Paraldehydum, Hyoscina Hydrobromidum *See also under Cocaine for numerous local, spinal and surface anæsthetics See also Hypnotics.*

**Anal Fissure.**—*Local*—A B A, B A B A N, Ichthammol, Quininæ et Ureæ Hydrochlor, Supp Iodof, Ung Atrop, Ung Bellad, Ung Cocain, Ung Conii, Ung Gall c Opio

**Analgesics or Anodynes.**—Acetanilidum, Acidum Acetylsalicylicum, Amidopyrina, Calci Acetylsalicylas, Colchicina, Hyoscina Hydrobromidum, Lithii Acetylsalicylas, Lithii Salicylas, Methylacetanilidum, Morphina, Opium, Papaveretum, Phenacetinum, Phenazoni Salicylas, Phenazonum, Quininæ Acetylsalicylas, Quininæ Salicylas, Salicinum, Sodii Salicylas

*Local*—Aconiti Folium, Aconitina, Aconitum, Belladonnæ Radix, Benzaminæ Hydrochloridum, Benzaninæ Lactas, Camphora, Chloralis Hydras, Chlorbutol, Eugenol, Menthol, Methylis Salicylas, Oleum Caryophylli, Orthocaina, Phenol *See also Anæsthetics, Local.*

**Anaphrodisiacs.**—Acidum Hydrobromicum Dilutum (and bromides), Belladonnæ Folium, Belladonnæ Radix, Camphora, Conii Folium, Conii Fructus, Hyoscina Hydrobromidum, Hyoscyaminæ Sulphas; Hyoscyamus, Stramonium

**Aneurism.**—Aconitum, Amylis Nitris, Calci Chloridum, Digitalis, Ergota, Iodoprotein, Liquor Glycerylis Trinitratis, Morphina, Potassii Iodidum, Veratrum

**Angina Pectoris.**—Aconitum, Æther, Æthylis Iodidum, Amylis Nitris, Digitalis, Erythritylis Tetranitras, Euphyllin, Liquor Glycerylis Trinitratis, Mannitylis Hexanitras, Morphina, Muscle and tissue extracts, Papaverina, Phenazonum, Pyridina, Theobromina, Theobromina et Sodii Salicylas, Theophyllina et Sodii Acetas

**Anhidrotics.**—Acidum Agaricum, Acidum Camphoricum, Atropina, Belladonnæ Folium, Belladonnæ Radix, Hyoscyamus, Picrotoxinum, Stramonium, Zinci Oxidum

*Local*—Acidum Aceticum Dilutum, Alcohol, Alumen, Aluminii Acetas, Aluminii Chloridum, Chromii Trioxidum, Liquor Formaldehydi, Trinitrophenol, Zinci Oxidum

**Ankylostomiasis.**—*See Anthelmintics.*

**Anodynes.**—*See Analgesics and Neuralgia.*

**Anorexia.**—Calumba; Capsicum; Cascarella, Chirata, Cinchona, Gentiana, Nux Vomica, Quassia; Quinina; Strychnina.

**Antacids** (*to diminish the acidity of the gastric contents*).—Aluminii Hydroxidum, Bismuthi Carbonas, Bismuthi Hydroxidum; Calci Carbonas, Calci Hydroxidum, Calci Phosphas; Creta; Magnesii Carbonas Levis, Magnesii Carbonas Ponderosus, Magnesii Hydroxidum; Magnesii Oxidum Leve, Magnesii Oxidum Ponderosum; Magnesii Phosphas, Magnesii Trisilicas, Potassii Bicarbonas; Sodii Bicarbonas.

*To increase the alkalinity of the blood.*—Dextrosom, Potassii Acetas; Potassii Citras; Sodii Acetas; Sodii et Potassii Tartras.

**Anthelmintics.**

*Hook-worm.*—Betanaphthol; Carbonei Tetrachloridum, Oleum Chenopodii, Tetrachlorethylenum, Thymol.

*Round-worm.*—Butæ Semen, Carbonei Tetrachloridum; Cucurbita; Hexyl-resorcinol; Hydrargyri Subchloridum, Naphthaleni Tetrachloridum, Naphthalenum; Oleum Chenopodii; Oleum Terebinthinæ, Santoninum, Spigelia, Tetrachlorethylenum.

*Tape-worm.*—Areca, Cucurbita; Cusso, Ext Filic, Granati Radicis Cortex, Kamala, Naphthaleni Tetrachloridum, Naphthalenum, Oleum Terebinthinæ, Pelletierinæ Tannas

*Thread-worm.*—Calci Permanganas, Carbonei Tetrachloridum, Ferri Sulphas, Oleum Chenopodii, Santoninum, Sulphur, Thymol. *Cathartics.*—Hydrargyri Subchloridum, Magnesii Sulphas, Oleum Ricini, Sodii Sulphas *Rectal Irrigation.*—Acidum Tannicum, Alumen, Calci Hydroxidum, Ferri Sulphas, Oleum Terebinthinæ, Quassia, Quininæ Bisulphas, Sodii Chloridum

**Anthrax.**—Neoarsphenamina, Sclavo's Serum

**Antilithics.**—Acidum Benzoicum (and salts), Formamol, Hexamina, Liq Pot Hydrox, Lithium salts, Magnesii Oxidum, Piperazina, Potassii Bicarbonas, Potassii Citras, Sodii Bicarbonas, Sodii Citras, Sod Citro-Tart Efferv, Sodii Phosphas, Urea

**Antiperiodics.**—Arseni Trioxidum, Berberinæ Sulphas, Cinchoninæ Sulphas, Ferri et Ammonii Citro-Arsenis, Narcotina, Phloridzinum, Picrorhiza, Piperina, Quinine salts, Salicinum

**Antipyretics.**—Acetanilidum, Acidum Acetylsalicylicum, Amidopyrina, Calci Acetylsalicylas, Cinchona, Lithii Acetylsalicylas, Phenacetinum, Phenazonum, Quinina, Quininæ Acetylsalicylas, Quininæ Disalicylosalicylas, Salicinum, Sodii Salicylas

**Antiseptics**—*General.*—Calci Oxidum, Calx Chlorinata, Naphthalenum (*In solution for utensils, excreta, bedding, etc*) Hydrargyri Perchloridum, Liq Cresol Sap, Phenol, Zinci Chloridum (*Gaseous for sick rooms, etc*) Chlorine, Cresol (vapour), Paraformaldehydum (vapourised), Phenol, Sulphur (ignited), Sulphuris Dioxidum

*Local (to sterilise the skin before operation)*—Acriflavina, Alcohol, Dettol and similar solutions Hexylresorcinol, Hydrargyri et Potassii Iodidum, Hydrargyri Oxycyanidum, Hydrargyri Perchloridum, Iodum, Liq Cresol Sap, Mercurochromum, Methylviola; Phenol; Trinitrophenol, Viride Nitens

*(For skin diseases)*—Acidum Boricum, Acidum Salicylicum, Acidum Sulphurosum; Acriflavina, Argenti Nitras, Argenti Proteinas, Benzenum; Betanaphthol, Bismuthi Tribromphenas, Chloramina, Chromii Trioxidum, Chrysarobinum, Dichloramina, Hydrargyri Iodidum Rubrum, Hydrargyri Perchloridum; Hydrargyrum Ammoniatum, Ichthammol, Iodoformum, Iodum, Liq Calc Sulphurat, Liquor Formaldehydi, Liquor Hydrogenii Peroxidi; Magenta, Mercurochromum, Methylthioninæ Chloridum, Phenol, Pix Carbonis, Pix Liquida, Proflavina, Pyrogallol, Resorcinol, Rubrum Scarlatinum; Sulphur Præcipitatum, Trinitrophenol, Viride Malachitum, Viride Nitens

*(For the eye)*—Acidum Boricum, Æthylhydrocupreinæ Hydrochloridum, Argenti Nitras, Argenti Proteinas, Cupri Sulphas, Hydrargyri et Zinci Cyanidum; Hydrargyri Oxidum Flavum, Hydrargyri Oxycyanidum, Ichthammol, Potassii Hydroxyquinolini Sulphas, Zinci Sulphas.

*(For the mouth and throat)*—Acidum Boricum, Argenti Nitras; Argenti Proteinas, Chloramina, Chromii Trioxidum; Eugenol, Garg Chlor, Hydrargyri Perchloridum, Liq Calc Chlorinat; Liq Cresol Sap; Liquor Hydrogenii Peroxidi, Liq Sod. Chlorinat Chir; Phenol; Potassii Chloras, Potassii Permanganas; Sodii Perboras; Thymol, Viride Malachitum, Viride Nitens, Zinci Chloridum.

*(For the nose)*—Acidum Boricum, Argenti Proteinas, Borax; Camphora, Liquor Hydrogenii Peroxidi; Menthol, Oleum Eucalypti, Thymol.

*(For the urethra and bladder)*—Acriflavina; Argenti Nitras, Argenti Proteinas; Hydrargyri Oxycyanidum; Mercurochromum, Potassii Hydroxyquinolini Sulphas, Potassii Permanganas, Proflavina; Viride Malachitum; Viride Nitens, Zinci Sulphas; Zinci Phenolsulphonas.

*(For the vagina)*—Acidum Boricum; Acriflavina; Argenti Proteinas; Dettol and similar solutions; Glycerinum; Hexyl-resorcinol; Hydrargyri Oxycyanidum;

Hydrargyri Perchloridum, Ichthammol, Liq. Cresol Sap; Magenta, Mercurochromum, Methylthioninæ Chloridum, Phenol, Potassii Permanganas, Trinitrophenol, Zinci Phenolsulphonas

(*For the rectum*)—Acriflavina; Argenti Nitras; Argenti Proteinæ; Potassii Permanganas

(*For open wounds*).—Acidum Boricum; Acriflavina; Euflavina, Hydrargyri et Zinci Cyanidum, Hydrargyri Iodidum Rubrum, Hydrargyri Perchloridum, Ichthammol, Liquor Hydrogenii Peroxidi, Liq Sod Chlorinat Chir, Potassii Permanganas, Trinitrophenol, Zinci Sulphas

**Antiseptics, Internal (Stomachic)**—Creosotum, Oleum Cubebe, Resorcinol.

(*Intestinal*)—Acidum Acetylsalicylicum; Betanaphthol, Bismuthi Salicylas, Creosotum; Euflavina, Guaiacol, Hydrargyri Perchloridum, Hydrargyri Subchloridum, Lac Coactum, Phenol, Potassii Guaiacolsulphonas, Salol; Thymol *See also Cathartics.*

(*Urinary*).—Acidum Mandelicum (and Salts), Ammonii Benzoas Buchu, Copaiba; Cubeba, Hexamina, Hexyl-resorcinol, Lithii Benzoas, Methylthioninæ Chloridum, Oleum Cubebe; Oleum Juniperis; Oleum Santali, Pyridium, Salol; Sodii Benzoas *To render the urine acid*—Acidum Hydrochloricum Dilutum, Ammonii Benzoas; Ammonii Chloridum; Ammonii Nitras, Sodii Phosphas Acidus *To render the urine alkaline*—Magnesii Hydroxidum, Potassii Bicarbonas, Potassii Citras, Sodii Bicarbonas, Sodii Citras, Sodii et Potassii Tartras

(*Respiratory*).—Creosotum, Cubeba, Potassii Guaiacolsulphonas, Terebenum  
**Antispasmodics. (Respiratory)**.—Adrenalina, Amyli Nitris, Atropina, Belladonna, Benzylis Benzoas, Chloroformum, Codeina (and salts), Diamorphinæ Hydrochloridum, Ephedrina (and salts), Hyoscyamus, Lobelia, Stramonium (*Intestinal*)—Atropina, Belladonna, Diamorphinæ Hydrochloridum, Codeina (and salts), Hyoscina, Hyoscyamina, Hyoscyamus, Morphina (and salts); Opium—*See also Asthma, Convulsions and Epilepsy.*

**Anuria, see Urine, Retention of.**

**Aortic Disease.**—Ammonii Carbonas, Inj Camph, Ferri Iodidum, Ferri Perchloridum, Iodides, Nux Vomica, Sodii Salicylas, Tab Erithrityl Tetranit, Tab. Glyc Trinit et Sod Iod c Arsen—*See also Angina Pectoris.*

**Aperients.**—Agar, Aloe, Cascara Sagrada, Conf Senn, Enema Aloes, Enema Mag. Sulph, Enema Ol Oliv, Enema Ol Ricin, Enema Ol Ricin c Sap, Enema Sap, Enema Terebinth, Euonymus, Fel Bovinum, Glycerinum, Hydrargyri Subchloridum, Hydrarg c Cret, Magnesii Carbonas Levis, Magnesii Carbonas Ponderosum, Magnesii Oxidum Leve, Magnesii Oxidum Ponderosum, Magnesii Sulphas, Manna, Oleum Amygdalæ, Oleum Olivæ, Oleum Ricini, Paraffinum Liquidum, Paraffinum Molle, Phenolphthaleinum, Pulv. Glycyrrh. Co., Pulv Efferv Co., Rhamnus, Rheum, Sapo Durus, Sennæ Folium, Senna Fructus, Sod Citro-Tart Efferv., Sodii et Potassii Tartras, Sodii Phosphas, Sodii Sulphas, Sulphur Præcipitatum, Sulphur Sublimatum, Supp Glycer, Syr Fic Co, Tamarindus *See also Cathartics.*

**Aphonia.**—*See Voice, Loss of.*

**Aphrodisiacs.**—Alcohol, Cannabis, Cantharidinum, Damiana, Nux Vomica, Phosphorus, Strychnina, Yohimbina *See also Debility and Nervous Debility.*

**Aphthæ.**—*See Stomatitis.*

**Arterial Tension, Raised**—Aconitum, Antimonial preparations, Muscle and tissue extracts, Potassii Iodidum, Pulv Sod Nitris Co, Sodii Thiocyanas, Veratrum Viride. *See also Arteriosclerosis, Blood Pressure and Vasodilators.*

**Arterial Tension, Lowered**—Pituitary preparations raise tension of the blood vessels *See Cardiac Tonics.*

**Arteriosclerosis.**—Acetylcholine subcutaneously; Adrenalina, Aspidrodine, Benzoates, Camphora; Citrates, Coramine, Iodoprotein, Lactic acid-forming bacilli preparations, Magnesii Sulphas, Muscle and tissue extracts; Potassii Iodidum, Sodii Sulphas, Sodii Thiosulphas, Strophanthus; Syr Iodotann; Tab Erithrityl Tetranit; Theobromina et Calcii Salicylas, Thyroid preparations  
**Depressor agents, e g.,** Hippurates; Potassii Iodidum, Tab. Glyc Trinit., Tab Sod. Nitrit. Co.; for pre-sclerosis, Diuretics, finally Theobromine and Digitalis

**Arthritis.**—*See Gout and Rheumatism.*

**Arthritis Deformans.**—*See also Rheumatoid Arthritis and Rheumatism, Chronic.* Iodine by ionisation; Sulphur injected. Peptone intramuscularly  
**Treat as in early phthisis.**—Creosotum; Guaiacol, Oleum Morrhuæ, tonics, hæmatics. Later, Iodine and Iodides



**Ascarides.**—*See Anthelmintics.*

**Ascites.**—*See Dropsy.*

**Asphyxia.**—Carboni Dioxidum and Oxygenum, Oxygenum. Schafer's prone pressure method is effected by pressing on the small of the back (thus compressing the abdominal viscera and pushing the diaphragm upwards) for 3 seconds, turning over on the right side for 3 seconds, and repeating until resuscitated. This allows mucus and water, in the case of drowning, to run from the mouth. Sylvester's, Howard's and older methods described—*Problems of Asphyxia*, Brit Assn Cent. Meeting, *Lancet*, ii/1931, 795

**Asthma.**—Acidum Hydriodicum Dilutum and Iodides, Acidum Hydrobromicum Dilutum and Bromides, Adrenalina (hypodermically), Æthylmorphinæ Hydrochloridum, Amylis Nitris; Arseni Trioxidum, Atropina, Belladonna, Benzyls Benzoas, Benzylmorphinæ Hydrochloridum, Caffeina, Chloralis Hydras, Cocaina, Codeina, Coniina, Diamorphinæ Hydrochloridum, Ephedrina, Euphorbia, Grindelia; Hyoscinæ Hydrobromidum, Insufflatio Adrenalinae, Liquor Glycerylis Trinitratis, Lobelia, Mist Lobel. et Stramon. Co., Moschus, Paraldehydum, Peptonum, Pilocarpina, Piscidia, Protein Therapy, Sanguinaria, Sodii Iodas; Sodii Nitris, Stramonium, Tinct Eucalyp. Sprays Neb Adrenal. Aromat.; Neb. Adrenal. et Cocain., Neb. Adrenal. et Ephed., Neb. Adrenal. et Ephed. Oleos.; Neb. Hyoscin. Co., Neb. Menthol. et Thymol. Co.

**Substances to be Burnt and the Fumes Inhaled.**—Belladonnæ Folium, Cannabis, Chart Nit., Lobelia, Potassii Nitras, Pulv. Lobel. Co., Pulv. Stramon. Co.; Stramonium; Tabacum.

**Vapours to be Inhaled.**—Æthyls Bromidum, Æthyls Iodidum, Amylis Nitris, Chloroformum, Pyridina, Vap. Eucalyp. Co.

**Astringents.** *Internal.*—Adrenalina, Ephedrina (by constriction of the arterioles); Acetannin, Acid Sulph. Dil.; Aluminii Hydroxidum, Bismuthi Carbonas; Bismuthi Subnitras, Bismuthi Tannas, Catechu, Catechu Nigrum, Cinchona, Cinnamomum, Creta, Guarana, Hæmatoxyllum, Kino Eucalypti, Krameria, Opium, Plumbi Acetas, Quercus

*Local.*—Acidum Lacticum, Acidum Tannicum, Alumen, Alumen Ferricum, Aluminii Acetas, Aluminii Hydroxidum, Argenti Nitras, Bismuthi Carbonas, Bismuthi Subgallas, Bismuthi Subnitras, Calamina, Calcii Hydroxidum, Cupri Sulphas, Ferri Perchloridum, Galla, Glycerinum (by absorption of water), Hamamelis, Kino, Kino Eucalypti, Krameria, Plumbi Acetas, Plumbi Carbonas; Plumbi Oleas, Potassii Chloras, Zinci Carbonas, Zinci Chloridum, Zinci Oxidum, Zinci Phenolsulphonas, Zinci Sulphas

**Atelactasis**, to prevent—Carboni Dioxidum and Oxygenum as prophylactic

**Atheroma.**—*See Arteriosclerosis.*

**Athlete's Foot.**—Castellani's Magenta Paint, Mycozol, Ung. Acid. Salicyl. **Auricular Fibrillation.**—Digitalis, Quinidinæ Sulphas. *See also Cardiac Tonics.*

**Bacilluria (B. Coli).**—Acidum Mandelicum (and salts), Argenti Proteinæ Mite, Hexamina and Sodii Phosphas Acidus (separately), Hexyl-Resorcinol, Oleum Santali, Pyridium, Vaccines, Make urine alkaline, e.g., with Potassii Bicarbonas or Sodii Citras

**Balanitis.** *Local.*—Acidum Tannicum, Lotions of Plumbi Acetas, Zinc salts, Silver preparations, Zinci Oxidum

**Baldness.**—*See Alopecia.*

**Basedow's Disease.**—*See Exophthalmic Goitre.*

**Bed-Sores.** *Local.*—Acidum Boricum, Acidum Tannicum, Alumen, Amylum, Balsamum Peruvianum, Iodoformum, Zinci Oxidum, (as prophylactics) Alcohol, Alumen (in a lotion)

**Beri-Beri.**—Cerevisiæ Fermentum, Vitamin B concentrates

**Bile, Deficiency of.**—*See Cathartics.*

**Bilharziasis.**—Antimonii et Potassii Tartras, Antimonii et Sodii Tartras, Emetinæ Hydrochloridum.

**Billousness.**—Chirata, Dextrosum, Euonymus, Ext. Euonym., Ext. Irid., Ext. Leptand.; Ext. Sanguin., Hydrargyri Subchloridum; Mag. Sulph. Efferv., Podophylli Resina, Pulv. Efferv. Co., Sod. Phosph. Efferv.; Sod. Sulph. Efferv. *See also Aperients and Cathartics.*

**Bites and Stings, Insects.** *Local.*—Ammonii Carbonas (in solution), Liq. Ammon. Dil.; Liquor Formaldehydi; Liq. Pot. Hydrox., Liq. Sod. Hydrox., Lot. Phenol.; Magnesi Sulphas (saturated solution), Oleum Citronellæ, Oleum

Eucalypti, Oleum Lavandulæ; Oleum Rusci, Sodii Bicarbonas (in solution), Sp Camph, Thymol, Tinct Pyreth Flor

**FLY PREVENTION.**—The following have been advised for destruction For *rubbish heaps*, etc.—Borax, Calci Boracis, Calci Hydroxidum, Calx Chlorinata; Potassii Permanganas For *use indoors*—Formalin, alcohol and water As *deterrents*—Cresol, Paraffinum; Phenol, Pyrethrum For *spraying outside walls or canvas of hospitals, etc*—Berlece's Solution (v infra) may be used Use in the evening or early morning Another formula is Liquor Formaldehydi 1 ounce, water  $\frac{1}{2}$  pint, milk  $\frac{1}{2}$  pint

To kill flies a 1% solution of Sodii Salicylas is better than Liquor Formaldehydi. Of the latter 1 25 to 2 5% of commercial Liquor Formaldehydi is the best strength

**Formaldehyde as a poison for house-flies**—Formula recommended, Liquor Formaldehydi 5, Aqua Calcis 50, Sacrosum 2 5, Aqua 42 5

Oleum Morrhuæ has a specific toxic action on all flies, mosquitoes and ticks Sprinkled on the surface of water, it is more effective than petroleum in the destruction of larvæ

Pastilles for burning have been advised, made of the following Phenol 6 drachms, Potassii Nitrates  $1\frac{1}{2}$  ounces, Pyrethri Flos Pulverata 5 ounces, Carbo 10 ounces and Mucil Trag q s A sponge dipped in Sp Camph will also impregnate the air and act as deterrent

Berlece's Solution—Sodii Arsenis 20 grammes, Theriaca 100 grammes, Aqua 1 litre Steep grass in this and hang it up

Veratrum Album Pulverata and Veratrum Viride Pulverata  $\frac{1}{2}$  lb to 10 gallons of water applied at the rate of this amount to 8 bushels of manure is an effective larvicide

**INSECTIFUGE** To prevent flies from settling on man and horses—Pyridina 1, Thymol  $\frac{1}{2}$ , Safrol 5, Oleum Rusci 5, Oleum Cetacei to 100 Does not irritate the skin A small quantity to be smeared on the temples, behind the ears and on the head or on leather of harness Kerosene is also effectual

The following spray solution should be useful Naphthalenum 10, Phenol 10, Camphora 5, Oleum Limonis 5, Oleum Thymi 2, Oleum Lavandulæ 2, Oleum Sabinæ 2, Spiritus Methylatus Industrialis to 500

Aloes is a local sedative, as is Tinct Benzoin Co A saturated solution in Tinct Tolu is good against insect bites.—F W Cock, *Brit med J*, ii/1918, 25

The black flies on the river banks in Canada are kept off by a mixture of Kerosene and Oleum Succini Oleum Pini is said to deter Anopheles See also *Malaria*, Vol II

**Local**—Liq Calc. Chlorinat, Potassii Permanganas

**Bitters.**—Alstonia, Andrographis, Anthemis, Aristolochia, Auranti Cortex, Azadirachta, Calumba, Cascarilla, Chirata, Cinchona, Coccinnum, Cusparia, Gentiana, Lupulus, Picrorrhiza, Quassia, Quebracha, Quinina, Serpentina

**Blackwater Fever.**—Atebrin, Caffeina et Sodii Benzoas, Digitalis, Hydrargyri Subchloridum, Methylthioninæ Chloridum, Neoarsphenamina, Plasmoquine, Quinina, Sal Efferv, Sodii Chloridum intravenously, Sternberg's mixture, Strychnina

**Treatment**—Keep patient warm, sponge with warm water, in case of pyrexia, sponge with cold water, with vinegar and lime juice added, keeping the brain cooled by compresses On signs of cardiac failure, small doses of champagne or brandy and soda water given—soda water could be taken *ad lib*. Warm blanket baths for delirium or rising temperature A mixture containing the following has been used with good results Sp. Ether. Nitros, Potassii Bicarbonas and Potassii Nitrates In case of bad malarial history or anæmia without such, 1-grain doses of quinine should be given in addition, alternating with mixture, as soon as stomach can stand it. Suggests trial of Thyroideum to stimulate lymphoid system.—G Rome Hall, *J. trop. Med. (Hyg)*, 1923, 120.

**Sternberg's Mixture**—Sodii Bicarbonas 10 gr., Lq. Hydrarg Perchlor 15 m, Aqua ad 1 oz. Every 2 hours for the first day and every 3 hours after until the urine clears.

The urine clears up more quickly with immediate subcutaneous injection of 5 to 10 oz. of Lq Sod. Chlorid. Physiol. and  $\frac{1}{2}$  to 1 oz. Magnesii Sulphas is beneficial. The following mixture every hour in 5 oz of water prevents nausea and restlessness: Sodii Bicarbonas 20 gr., Bismuthi Carbonas 10 gr.; Tinct. Chlorof. et Morph. Co. 5 m. (Sternberg's Mixture causes vomiting.) Large quantities of fluid should be given, and patient should not be moved for at least 14 days.—E. P. Carmody, *Brit. med J.*, i/1925, 106.

Give alkalis as follows: Sodii Bicarbonas 2½ oz., Calcii Carbonas 5 oz., Magnesii Carbonas 5 oz., and Bismuthi Carbonas 10 dr. One teaspoonful every 2 hours in water from 6 a.m. to 10 p.m. and then a double dose. Boiled water freely every ½ hour. Absolute rest. 3 or 4 doses of Hydrargyri Subchloridum ½ grain at ½-hour intervals. Soap and water enema at onset, and enemas of weak Potassii Permanganas twice daily. If temperature like subtertian fever, and parasites are found, give 1 dr. Tinct. Cinchon thrice daily, carefully increased in a day or two, and if no recurrence of blackwater add Quininæ Dihydrochloridum. If hæmoglobinuria develops, stop all food and give nothing but boiled water till urine is clear for 3 days and alkaline in reaction. This only fails where vomiting uncontrollable, when alkalis intravenously may save patients.—J. Forbes, *Trans R Soc trop Med*, Nov 25, 1929, 317; *J. Amer. med. Ass.*, ii/1929, 1686.

**Bladder Affections.**—See Antiseptics, Urinary, and Cystitis.

**Blastomycosis.**—Acidum Salicylicum; Hydrargyrum Ammoniatum, Iodoformum. Carbonei Dioxidum snow Saline intravenously—1500 ml. See also Vol II.

**Bleeding of Gums.**—See Gums, Inflamed and Spongy.

**Bleeding, to arrest.**—See Hæmorrhage and Epistaxis.

**Bleeding from Leech Bites.**—Adrenalina, Alumen; Collod. Stypt., Liq. Ferr. Perchlor. See also Hæmorrhage.

**Blepharitis.**—See Conjunctivitis.

**Blistering Applications.**—See Counter-irritants (vesicants).

**Blood Pressure, to increase.**—See Vasoconstrictors.

**Blood Pressure, to reduce.**—See Vasodilators. Phenobarbitone lowers pressure and has sedative effect. The thiocyanates are of value in doses of 1½ to 2 grains thrice daily after food, the dose being increased daily.—John Hay, *Brit. med. J.*, ii/1931, 47.

A raised cholesterol content the most constant blood change found—often above 200 mg per 100 ml. Veratrone, ½ to 1 ml intramuscularly, or *per os*, of value, but must be used with caution as fall of blood pressure may be alarming in susceptible patients. Acetylcholine intravenously also of value—0.05 g increased to 0.1 g daily, but extremely dangerous. Venesection still unsurpassed. In the shallow, toxic type, pilocarpine ½ grain hypodermically 6 or 12 days, followed by hot, wet pack and massage, with colon lavage twice weekly, fruit and fish diet and Vichy before meals.—A. H. Douthwaite, *Brit. med. J.*, ii/1929, 844-847.

**Table salt in hyperpiesis.** When renal, cardiac or cerebral complications are present, give non-pressor table salt, if craving is felt, consisting of Ammonii Hippuras 1, Potassii Nitrates 4, Potassii Chloridum 25. In emergencies, as threatened or actual apoplexy, lumbar puncture. Venesection up to 500 ml, followed by fasting for a couple of days, gives relief. For toxæmia resulting from intestinal stasis, Potassii Permanganas 1 grain *per rectum* in a pint of water every morning for 3 weeks, with Hydrargyri Subchloridum 2 grains at night twice weekly, followed by saline *mane*. In lesser grades, Potassii Chloridum 2 grains t.d. in a tumbler of water. For cardiac types, Theominal is diuretic and lowers pressure. Iodides of little use. Tinct. Iod. (French) 5 minims in water or milk p.c. better. Sodii Thiocyanas, 3-grain tablets *per os*, where organic changes in the arteries are absent. Choline derivatives, *per os*, and Acetylcholine Hydrochloridum parenterally. Animsa, a muscle extract, of benefit in sclerotic cases.—J. F. Halls Dally, *Brit. med. J.*, ii/1930, 10. Vegetarian diet not ideal. Butcher's meat might be allowed two or three times a week. Copious amounts of fluid not good. Iodides head list of useful drugs. Digitalis (though paradoxical) often good.—Sir T. Horder, *Brit. med. J.*, i/1930, 741.

**Blood Tonics.**—See Hæmatinics.

**Boils and Carbuncles.** *Internal.*—Acidum Nucleicum; Acid. Sulph. Dil., Arseni Trioxidum, Calx Sulphurata; Cerevisiæ Fermentum, Ferri Sulphas; Magnesii Sulphas; Mangani Butyras; Potassii Bicarbonas; Sodii Arsenas Anhydrosus, Sodii Bicarbonas; Stanni Oxidum; Vaccinum Staphylococcicum (hypodermically); whole blood injections.

*Local.*—Acid Boricum, Cataplasma. Kaolin; Glycer. Atrop.; Glycer. Bellad.; Iodum; Liquor Hydrogenii Peroxidi, Pasta Mag. Sulph.; Sp. Camph.

**Botulism.**—Serum Antibotulinum. See also Vol. II.

**Breasts, Inflammation of.**—Atropina; Belladonna.

**Breath, Fetid.**—Acid Salicylicum; Calcii Permanganas, Camphoræ; Liq.

Formaldehydi preparations; Mist Mag Hydrox, Potassu Permanganas, Tab Formaldehydi to suck; Tinct. Myrrh. et Borac, Vapor Creosot

**Bright's Disease.**—See **Nephritis**.

**Bromidrosis.**—Potassu Permanganas wash, weak solution of Liquor Formaldehydi

**Bronchiectasis.**—Acid Sulph Dil., Hydrargyri Salicylas, Inhal Creosot  
*Diagnosis*, Oleum Iodisatum

**Bronchitis.** *Internal*—Acalypha, Aconitum, Aethylmorphinæ Hydrochloridum, Allylis Sulphidum, Ammoniacum, Ammonii Acetas, Ammonii Benzoas, Ammonii Carbonas, Ammonii Chloridum, Antimonials, Apomorphinæ Hydrochloridum, Asafœtida, Benzylmorphinæ Hydrochloridum, Copaiba, Diamorphinæ Hydrochloridum, Galbanum, Guaiacolis Valerianis, Ipecacuanha, Lobelia, Morphina, Papaverina, Pix Liquida, Potassu Iodidi, Prunus Serotina, Scilla, Terebentum, Terpinii Hydras.

*Local*—Cataplasma Sinap, Chart Sinap, Gossypium Capsici, Lin Ammon, Lin Camph, Lin Succin Co, Neb Cocain Co, Neb Iod Co, Neb Iod et Menthol, Neb Menthol et Thymol Co, Oleum Terebinthinæ (in an inhalation), Ung Capsic Fort, Vap Conii, Vap Creosot, Vap Cubeb, Vap Eucalypt, Vap Eucalypt Co, Vap Iod, Vap Iod Ether, Vap Ol Pini

*Bronchial Secretion is increased by*—Alkalis, especially Ammonii Carbonas and other Salts of Ammonium, Apomorphina, Balsamum Peruvianum, Balsamum Tolutanum, Benzoinum, Camphora, Iodum, Ipecacuanha, Jaborandi, Oleum Terebinthinæ, Pix Liquida, Potassu Iodidum, Quillaia, Scilla, Senega, Sulphur, Terebentum

**Bronchocele.**—See **Goitre**.

**Broncho-Pneumonia** and capillary bronchitis in infants —Mist Paraldehyd and Potassu Iodidum, Spiritus Frumenti in small doses Emetine hypodermically. Glucose feeding *per rectum*.

**Bruises.**—Ammonii Chloridum (in a lotion), Anthemis (as a fomentation), Liq Hamam, Liq Plumb. Subacet Dil, Lin Sap, Lot Plumb c Opio, Lotio. Plumb Evap, Tinct Arnica Flor, Tinct Arnica Rad, Tinct Calend

**Burns and Scalds.**—Acidum Tannicum, Acriflavina, Cocaina, Lin Calamin, Lin Calc. Hydrox, Lin Calc Hydrox c Ol Lini, Lot Trinitrophen, Oleum Lini, Oleum Morrhuæ, Oleum Olivæ, Rubrum Scarlatinum, Sodii Bicarbonas, Thymol, Ung Acid Boric, Ung Cret, Ung Plumb Carb, Viola Crystallina

**Calculi, Biliary.**—Acidum Oleicum, Alkalis, Caps Sod Oleat Co., Fel Bovinum, Sapo, Sodii Benzoas, Sodii Bicarbonas, Sodii Glycocholas, Sodii Oleas

**Calculi, Urinary.**—Acid. Acet Dil douche, Agropyrum, Alkaline Carbonates, Ammi Viscosa, Ammonii Benzoas, Ammonii Phosphas, Aqua Destillata, Aqua Calcis, Lithii Citras, Mineral Acids (for phosphatic calculi); Piperazina, Potassu Citras, Sodii Benzoas, Sodii Hippuras, Sodii Phosphas Acidus, Vitamin A.

**Cancer.** *For Palliative Treatment*—Alnus Glutinosa, Arsenic preparations, Caps. Aldehyd. Cinnamic; Chelidonium, Chloralis Hydras and Opium preparations (as sedative), Condurango, Copper, colloidal; Ext Viola Liq, Fluorescentum Solubile and irradiation, Glucosum Liquidum feeding, Lead, colloidal, Plumbi Acetas; Selenium, colloidal; Sodii Cinnamas; Sodii Oleas *For Palliative Local Use*—Acetonum, Acidum Lacticum; Acidum Salicylicum cum Oleo, Arsenii Trioxidum; Chromii Trioxidum, Cobra venom, Coley's Fluid, Emp Cupr. Oleas, Glycerinum intravenously with Stannoxyl as adjuvant (Shirlaw), Glycer Phenol; Liq Calc. Chlorinat c Acid Boric, injected, Liquor Formaldehydi plugging and injection, Fig. Cupr. Sulph., Phenol (caustic) See also *Cancer and X-Ray and Radium Therapy, Vol. II*

**Cancerum Oris.**—Arsenicals

**Carbuncles.**—See **Boils**.

**Cardiac Tonics.**—Adrenalina, Caffaina, Camphora, Cardatone, Cardiazol, Crataegus, Coramine; Digitalis Folium; Liquor Glycerylis Trinitratis; Pituitarium; Scilla, Sparteinæ Sulphas; Strophanthus (Strophanthinum intravenously), Strychnina, Thyroideum; Veratrum Viride.

*Drugs acting upon the heart directly*—The force of contraction may be increased by—Apocynum; Barii Salts; Convallaria, Digitalis Folium; Erythrophæum; Physostigmina; Scilla; Sparteina; Strophanthus; Suprarenalium preps., Veratrum. Rate of the cardiac beat is increased by Ether; Alcohol; Anæsthetics; Chloroformum; Quinina. The vagus centre is stimulated by—Acidum

Hydrocyanicum; Aconitum, Adrenalina, Æther, Alcohol, Apocynum; Atropina, Butylchloralis Hydras, Chloralis Hydras, Chloroformum, Cocaina, Digitalis Folium, Extractum Pituitarii Liquidum; Hydrastis, Hyoscyamina (early in the inaction); Nicotina; Picrotoxinum, Scilla, Staphisagria (Delphumina), Strophanthus, Strychnina; Veratrina

Strychnine has little or no direct action; Pituitary has no direct action, but is truly a stimulant because of arteriole contraction and probable effect on capillaries. Camphor and compounds have a different foundation—detectable in failing heart. According to Trendelenburg they may be actually harmful in heart failure—*Lancet*, 11/1929, 1049

**Cardiac Depressants.**—Both force and the number of beats are decreased by—Acetanilidum, Acidum Hydrocyanicum; Aconitum, Antimony, Arsenic, Bromides, Chloralis Hydras, Emetina, Lobelia, Phenacetinum, Phenazonum

The vagus may be depressed by large doses of many of the above drugs, and drugs which diminish the blood pressure, such as Amyli Nitris and Cocaina

**Carminatives.**—Æther, Alcohol, Anethum, Anisum, Anthemis, Auranti Cortex, Camphora; Capsicum, Cardamomum, Carum, Caryophyllum, Cassia Cortex, Chloroformum, Cinnamomum, Coriandrum, Cuminum, Fœniculum, Menthol, Myristica, Oleum Anethi, Oleum Anisi, Oleum Anthemidis, Oleum Cari, Oleum Caryophylli, Oleum Cinnamomi, Oleum Coriandri, Oleum Fœniculi, Oleum Lavandulæ, Oleum Menthæ Piperitæ, Oleum Menthæ Viridis, Oleum Myristicæ, Pimenta, Zingiber

**Cataract, to prevent Senile.**—Iodides, Mercurials (Hydrargyri Cyanidum), Senecio. Bathing the eyes with a lotion of Calci Chloridum 4, Sodii Iodidum 4, Aqua 500

**Catarrh, Bronchial.**—*See* Bronchitis.

**Catarrh, Gastro-intestinal.**—*See* Gastritis.

**Catarrh, Nasal.**—Alumen (as insufflation), Anti-catarrhal vaccines, Belladonna, Benzadrine, Bismuthi Carbonas, Bismuthi Salicylas, Bismuthi Subnitras (as insufflation), Camphora, Elix Quinin Ammon Co, Glycer Thymol. Co, Gossyp, Menthol Co, Hydrastis (in lotions), Insuff Bism et Morph, Insuff. Menthol, Insuff Menthol et Cocain, Liquor Formaldehydi, Liquor Hydrogenii Peroxidi, Liq. Thymol Co., Menthol, Neb Adrenal Aromat; Neb. Adrenal et Cocain, Neb. Alk Co., Neb. Benzoin Co, Neb. Cocain Co, Neb. Ephedrin Co; Neb. Eucalypt; Neb. Eucalypt et Menthol et Cocain; Neb. Eucalypt et Pini, Neb. Iod. Co., Neb. Menthol et Thymol Co., Neb. Sod. Chlorid Co, Oleum Cinnamomi (in a spray), Oleum Eucalypti (inhaled), Oleum Picis (in an inhalation), Pig. Menthol Co, Pulv Borac Co (in a nasal douche), Quinina, Sodii Bicarbonas (in a spray), Vap. Ammon Chlorid., Vap. Eucalypt Co; Vap. Ol Pini

**Catarrh, Uterine.**—Acetarsol, Acid Tannic, Glycerinum, Glycer. Borac, Glycer. Phenol, Glycer. Plumb. Subacet, Opi et Amyli Enema, Phenol c. Camph., Ung. Adrenal., Zinci Sulphas uterine pencils and with Alumen. Zinc and other ions.

**Catarrh, Vesical.**—*See* Cystitis.

**Cathartics (Cholagogues)**—Acidum Nitro-hydrochloricum Dilutum, Acidum Oleicum, Fel Bovinum, Hydrargyri Subchloridum, Magnesii Sulphas, Oleum Olivæ, Podophylli Resina, Sapo Durus, Sodii Salicylas, Sodii Taurglycocholas (*Laxatives*).—Cassia Fructus, Euonymus, Ficus, Sulphur Præcipitatum, Sulphur Sublimatum; Tamarindus

(*Softening and bulk producing*)—Agar, Ispaghula, Linum, Paraffinum Liquidum, Paraffinum Molle; Psyllium; Tragacantha.

(*Saline Aperients*)—Magnesii Carbonas Levis, Magnesii Carbonas Ponderosus; Magnesii Hydroxidum; Magnesii Oxidum Leve, Magnesii Oxidum Ponderosum; Magnesii Sulphas, Potassii Tartras Acidus; Sodii et Potassii Tartras; Sodii Phosphas, Sodii Sulphas.

(*Acting on the colon*)—Aloe, Aloinum, Cascara Sagrada, Rheum, Sennæ Folium; Sennæ Fructus

(*Acting on the small intestine*).—Oleum Ricini; Phenolphthaleinum

(*Drastic Purgatives*).—Aloe; Aloinum; Cambogia, Colocynthis, Hydrargyri Subchloridum; Hydrargyrum, Ipomœa; Jalapa; Jalapæ Resina; Jalapin, Kaladana, Leptandra; Magnesii Sulphas, Oleum Crotonis, Oleum Ricini, Podophylli Resina, Podophyllum; Scammonæ Resina; Turpethum.

(*By hypodermic injection*).—Ergotoxina; Extractum Pituitarii Liquidum, Physostigmina.

(*Per rectum*).—Fel Bovinum; Glycerinũ; Oleum Olivæ; Sapo Durus.

**Caustics.** (*By consuming the tissue*)—Acidum Aceticum Glaciale, Acidum Hydrochloricum; Acidum Nitricum, Acidum Salicylicum; Acidum Sulphuricum, Acidum Trichloracetum, Calciu Oxidum, Chromii Trioxidum, Potassii Hydroxidum, Sodii Hydroxidum

(*By precipitation of protein*)—Alumen Exsiccatum; Aluminium Sulphas, Argenti Nitras, Cupri Nitras, Cupri Subacetat, Cupri Sulphas; Liquor Antimonii Chloridi, Phenol, Zinci Chloridum

(*By inflammation, producing a slough*)—Carbonei Dioxidum (solid)

**Cellulitis.**—Glycerin in conjunction with Liq Hydrarg Perchlor

**Cerebrospinal Meningitis.**—Serum Antimeniugococcicum

**Chancres, Soft.**—Antimonii et Potassii Tartras intravenously, Arsphenamina; Bismuthi Benzoas.

**Local**—Acidum Iodicum; Hydrargyri Subchloridum, Iodoformum, Liquor Hydrogenii Peroxidi, Liq Pic Carbon, Liq Plumb Subacet Dil, Lot Hydrarg Flav, Lot Hydrarg Nig, Mercurochromum, Resorcinol, Ung Iodof

**Chapped Hands.**—Adeps Lanæ, Glycer Amyli, Glycer et Aq Ros c Borac, Oleum Amygdalæ, Ung Acid Boric, Ung Aq Ros, Ung Borac, Ung. Camph Dur

**Cheiropompholyx** (Dermatitis between the fingers, previously called *Dyshidrosis*)—Liquor Formaldehydi a drachm to a pint of water as wash for hands, without drying, or Acidum Benzoicum and Acidum Salicylicum equal parts in Adeps Lanæ (15 grains aa to 1 oz) or Ung Hydrarg Ammon Dil 10 grains to 1 oz, or Argenti Nitras, 2 grains in Sp Æther Nitros 1 oz, applied to the papules when first appearing, often aborts —*Brit med J*, 11/1930, 626

**Cheyne-Stokes Respiration.**—Histamina

**Chicken-pox.**—See *Varicella*.

**Chilblains.** *Internal*—Calciu Chloridum, Calciu Iodidum, Calciu Lactas, Magnesii Oxidum Leve; Magnesii Oxidum Ponderosum, Magnesii Carbonas Levis, Magnesii Carbonas Ponderosus

**Local**—Capsicum; Chloral Camph, Cocaina, Collod Aceton, Collod Atrop, Colod Iod, Glycer Amyli, Ichthammol, Iodum, Lin Bellad; Lin Camph Ammon, Lin Capsic, Liquor Hydrogenii Peroxidi, Oleum Terebinthinæ, Ung Acid Boric, Ung Borac, Ung Bism, Ung Cadm Iod, Ung Camph., Ung Glycer Plumb Subacet, Ung. Phenol.

Thyroid and large doses of iodine is usually of great value Give calcium, parathyroid and Oleum Morrhuæ in the thin hypotonic scrofulous patient with acroasphyxia Obese people preferably treated with thyroid and Liq Iod Aq, but thin people do best on calcium Chilblains unbroken—paint with Tinct Capsic and Lin Camph Co equal parts For broken—Ung Coloph  $\frac{1}{2}$  oz, Ung Phenol.  $\frac{1}{2}$  oz, Zinci Oxidum 2 drachms, Paraffinum Molle to 2 oz For irritation—Liq Plumb Subacet Fort 2 dr, Lin Camph Ammon 6 dr, Oleum Sinapis Volatile 2 m Shake in a bottle. To be freshly made

**Chlorosis.**—Acidum Cacodylicum (and salts) Arseni Trioxidum, Guaiacol, Hæmoglobinum, Ferri salts, Mangani salts, Medulla Rubra, Potassii Permanganas, Sodii Arsenas Anhydrosus and other arsenates.

**Cholagogues.**—See *Cathartics*.

**Cholecystitis.**—See *Gall-bladder*.

**Cholelithiasis.**—See *Gall-stones*.

**Cholera.**—Acid Sulph. Aromat, Acid Sulph Dil, Bismuthi compounds, Camphora, Capsicum, Cholera bacteriophage, Coto, Cotoinum, Cupri Sulphas, Hydrargyri Subchloridum; Kaolinum, Liq Sod Chlor Physiol, Mist Cret Co, Morphina; Opium; Plumbi Acetas, Pil Plumb. c Opio, Salol, Tinct. Chlorof. et Morph Co, Vaccine, anti-cholera

**Chordee.**—Aconitum; Belladonna, Bromides, Camphora, Cannabis, Chloralis Hydras; Hyoscina, Hyoscyamina, Inj Morph hypodermically, Liq. Cantharidin (1 minim hourly), Supp Opio

**Chorea.**—Acidum Acetylsalicylicum, Acidum Salicylicum, Antimonials, Arseni Trioxidum; Bulbocapnina; Cacodylates, Calciu Acetylsalicylas, Calciu Chloridum; Calciu Lactas; Calciu Phosphas, Camphoræ Monobromidum, Cannabis and Chloralis Hydras, Carbromalum, Chloralis Hydras, Cimicifuga, Codeina, Conium and Coninæ Hydrobromidum, Ext. Cimicif Liq, Ferri Bromidum; Ergota, Ferri Phosphas; Formates, Gelsemium preparations; Hexamine intravenously; Hydrargyri Perchloridum; Hyoscine Hydrobromidum; Iodides, Iodoprotein, Lithii Acetylsalicylas, Magnesii Acetylsalicylas, Magnesii

Sulphas, Nirvanol; Oleum Morrhuæ, Tab. Glycer. Trinit., Phosphorus; Phytostigmina; Sodii Salicylas; Strychnina, Sulphonal; Valerianates; Zinci Bromidum; Zinci Oxidum, Zinci Sulphas.

**Cicatricial Tissue.**—Inj. Thiosinam et Phenazon., Inj. Thiosinam. et Sod Salicyl.; Thiosinam et Ethyl Iodid., Ung. Thiosinam et c. Phenazon., Urea

**Cirrrosis of Liver.**—Acid. Nitro-hydrochlor Dil., Ammonii Chloridum, Iodides, Mag. Sulph., Sodii Phosphas

**Climacteric Disorders.**—See **Menopause.**

**Clotting of Milk.** To prevent formation of clots in stomach—Sodii Citras Cold, Common.—See **Catarrh, Nasal.**

**Colic, Intestinal.**—Atropina; Benzylis Benzoas, Oleum Ricini; Opium; Tinct. Chlorof. et Morph. See also **Carminatives.**

**Colic, Lead.**—Acidum Sulphuricum Dilutum, Chloroformum (inhaled), Liq. Atrop. Sulph., Magnesi Sulphas, Potassii Bromidum, Potassii Iodidum, Sodii Sulphas, Tinct. Chlorof. et Morph. See also **Antidotes to Lead Poisoning**, p. 789.

**Colic, Renal.**—Amylis Nitris (inhaled), Cannabis, Chloroformum (inhaled), Collinsomia, Opium

**Colitis.**—Bismuthi Salicylas; Glucosum Liquidum, subcutaneous and intravenous injection, Hydrastis, Ispaghula, Kaolinum, Methylthioninæ Chloridum, Naphthaleni Tetrachloridum, Naphthalenum, Psyllium, Salicylates, Salol, Sodii Ricinoleas, Vaccinum Bacillus Coli, Zinc and other ionisation

**Colitis, Mucous.**—Astringents, e.g., Acidum Tannicum and Argenti Nitras, and sedatives, Betanaphthol, Bismuth salts, Kaolinum, Salol. Saline transfusion. Empty colon by lavage. Bismuth carbonate (2 ounces) in bread and milk every week. Where much fermentation add an ounce of charcoal. For clearing the bowel, castor oil.

**Colitis, Ulcerative.**—Argenti Salts, Bismuthi Carbonas, Calx Sulphurata, Ipecacuanha, Methylthioninæ Chloridum, Potassii Permanganas, Serum Antidysentericum, Vaccines.

Enema Bism. Subgall.; Oleum Morrhuæ cum Creosotum, Emuls. Sulphur injected through an artificial anus.

Direct treatment of the colon essential. Starch and opium enema, simple colonic washes with sodium chloride 1 drachm to 1 pint, or sodium bicarbonate 2 drachms to pint. Albargin enema, 20 grains in 30 ounces normal saline increased to 30 grains.—H. L. Tidy, *Brit. med. J.*, 1/1930, 135.

Charcoal, tannin (locally 1 or 2 grains to 1 ounce) given after preliminary lavage with low pressure by means of soft catheter, hydrogen peroxide 1 drachm to the pint without lavage may be better than tannin. Serum Antidysentericum.—A. F. Hurst, *Brit. med. J.*, 1/1931, 693, *Lancet*, 1/1921, 636.

**Collapse and Fainting.**—Adrenalina, Ether (hypodermically), Alcohol, Ammonii Carbonas; Camphora (hypodermically), Inj. Strych.; Liq. Glycerylis Trinitras, Mist. Ether. c. Ammon., Sp. Ether, Sp. Ammon. Aromat., Spiritus Frumenti, Spiritus Vini Gallici.

**Comedones.**—Calx Sulphurata, Ichthammol, Resorcinol, Sodii Peroxidum (in a paste), Vaccinum Staphylococcicum. See also **Acne.**

**Conjunctivitis.**—Acidum Boricum, Argenti Nitras, Argenti Proteinæ, Mucil. Sassaf. Medull., Oculent. Flav., Ung. Hydrarg. Oxid. Flav., Zinci Sulphas.

**Constipation.**—See **Aperients** and **Cathartics.**

**Convulsions.**—Amylis Nitris; Anæsthetics; Camphoræ Monobromidum, Chloralis Hydras, Chloralis Hydras and Morphina; Chloroformum, Conii Folium; Morphina; Moschus; Podophylli Resina; Potassii Acetas, Potassii Bromidum, Ruta, enema of (for infantile), Santoninum, Soda Bromidum; Sodii Nitris, Syr. Pot. Brom. et Pilocarp.; Supp. Chloral.

**Convulsions, Puerperal.**—See **Eclampsia.**

**Cornea, Inflammation and Ulcers of.** Local.—Acidum Boricum, Argenti Iodidum Recens; Atropina, Belladonna, Cocainæ Hydrochloridum, Duboisina, Fluoresceinum Solubile (diagnostic), Hydrargyri Subchloridum, Inf. Abri, Liq. Iod. Mit. (cocaine before and after, painted on); Mercurochromum; Phytostigmina; Pilocarpina and Quinina (as a lotion); Rubrum Scarlatinum and Atropina in Oleum Ricini, Ung. Hydrarg. Oxid. Flav.

Successfully treated with atropine and bandage and silvering of the lids. Septic and hypopyon ulcers are cauterised with camphor and phenol (equal parts), and paracentesis of anterior chamber repeated as required. Iodine injections intravenously hasten cure.—E. R. Shetti, *Brit. med. J.*, 11/1930, 1098.

**Corns.**—See **Warts.**

**Corpulence.**—See **Obesity.**

**Coryza.**—See **Catarrh, Nasal.**

**Cough.**—Acacia, Acidum Hydrocyanicum Dilutum, Æthylmorphinæ Hydrochloridum; Althæa, Amygdala Dulcis; Amygdalinum, Anisum; Balsamum Tolutanum, Chloroformum; Chondrus; Codeinæ Salts; Diamorphinæ Hydrochloridum, Elix. Diamorph. et Pin. Co., Glycerinum, Glycyrrhiza, Ipecacuanha, Lactuca, Lactucarium, Linum; Marrubium; Mist Chlorof Co, Morphina; Oleum Anisi, Opium, Oxytel; Papaveris Capsula, Pix Liquida; Prunus Serotina, Scilla, Senega; Terpin Hydras, Tinct. Chlorof et Morph; Tussilaginis Folium, Urtica

**Counter-irritants.**

**Rubefacients.**—Acidum Aceticum, Alcohol, Camphora, Cantharidinum, Cantharis, Capsicum, Chloroformum, Eucalyptol; Methylyl Salicylas, Liq Ammon Dil; Oleum Capuputi, Oleum Camphoræ Rectificatum, Oleum Myristicæ, Oleum Sassafras; Oleum Sinapis Volatile, Oleum Succini, Oleum Terebinthinæ, Oleum Thymi, Sinapis

**Vesicants.**—Cantharidinum, Cantharis, Carboni Dioxidum (solid), Oleum Crotonis, Oleum Sinapis Volatile, Sinapis

**Cretinism.**—Thyroideum preparations

**Croup, False.**—See **Laryngismus Stridulus.**

**Cuts.**—See **Abrasions.**

**Cystinuria.**—See **Calculi.**

**Cystitis.**—Acidum Boricum, Acidum Camphoricum, Acidum Lacticum, Acidum Mandelicum, Aconitum, Agropyrum, Alkalis, Ammonii Benzoas, Belladonna, Benzoates; Betanaphthylis Salicylas, Buchu, Collinsonia, Copaiba, Gokhru; Hexamuna, Hexaminæ Benzoas, Hexaminæ Salicylas, Hexyl-resorcinol, Hydrastis; Juniperus, Liq. Pot Hydrox, Magnesi Borocitras; Oleum Santali, Pareira, Salol, Sodii Salicylas, Sorghum; Uva Ursi, Vaccinum *B. coli* or appropriate vaccine

**Local.**—Argenti Fluoridum, Argenti Iodidum, Argenti Nitras; Bacillus Acidi Lact., Cocainæ Lactas, Enema Iod, Liq Formaldehyd Sap., Mercurochromum, Quininæ Bisulphas 1 in 2000, Argent Colloid, Hydrarg Colloid, Zinci Sulphanilas

**Acute Cystitis.**—Phenacetinum and Ext Hyoscy Sicc, Appropriate vaccine

**Local.**—Instillations, irrigations with Argenti Proteinæ, Potassii Permanganas (1 in 2000), etc

**Dandruff.**—See **Seborrhœa.**

**Debility.**—Acid Phosph Dil, Alcohol, Arsenic preparations, Arseni Trioxidum, Ext Medull Rub, Calcii Glycero-phosphas cum Lactæ, Calcii Hypophosphis, Hæmoglobin, Caps Valerian, Cinchona preparations, Elix Ferro-Mang Pept, Elix Gent Acid, Elix Hæmoglob c Ovolecithin, Emuls Ol Morr c Ovolecithin, Extractum Malti, Ext Malt. Ferrat, Ext Malt. Liq. c Glycero-phosph, Ext Malt. Liq c Hæmoglob, Ext Malt Liq c Hypophosph, Ext Malt Liq c Pancreatin, Liqueur Vitaminæ A, Mist Bism. et Pancreatin, Oleum Morrhuæ, Ovolecithinum, Pil Phosphor, Pil Ovolecithin, c Ferri Iod, Pil Potentum Co, Pulv Glycero-phosph Co, Quassia, Quinine preparations, Sodii Cacodylas, Strychninæ Cacodylas, Strychninæ Formas, Syr Ferri Phosph c Quinin, et Strych, Syr Glycero-phosph Co et c Format, Syr Kolæ Co  
See also **Anæmia.**

**Delirium Tremens.**—Ammonii Bromidum and other bromides, Camphoræ Monobromidum, Chloralis Hydras, Hyoscine Hydrobromidum, Hyoscine Sulphas See also **Dipsomania.**

**Demulcents.**—Acacia, Agropyrum, Althæa, Amygdala Dulcis, Cetraria, Chondrus, Gelatinum, Glycerinum, Glycyrrhiza, Linum; Maranta, Mel Depuratum, Oleum Amygdalæ, Oleum Arachis, Oleum Olivæ, Oleum Sesami, Tragacantha, Tussilaginis Flos, Ulmus Fulva

**Dengue Fever.**—Caffeina et Phenacetinum, Potassii Iodidum, Salicinum, Sodii Salicylas

**Dentifrices.**—Calcii Carbonas; Calcii Perboras, Cret c Camph, Diatomite, Iridis Rhizoma, Mag Perox. c. Cret., Os Sepiæ, Sodii Perboras.

**Deodorants.**—Acet. Odorat, Aluminii Acetas, Calx Chlorinata; Carbo, Chromii Trioxidum, Creosotum, Cresol, Guaiacol, Liqueur Formaldehydi, Liqueur Hydrogeni Peroxidi, Oleum Eucalypti, Oleum Picis; Potassii Hydroxyquinolini Sulphas; Potassii Permanganas, Sodii Perboras; Sp. Colon.; Terebinthum; Thymol. See also **Antiseptics.**



**Depilatories.** *Internal.*—Thalli Acetas *Local*—Baryta Sulphurata; Calx Sulphurata, X-Rays.

**Derbyshire Neck.**—See Goitre.

**Dercum's Disease.**—Thyroideum.

**Dermatitis.**—*Local*—Acidum Ascorbicum (by injection), Calamina; Liq. Alumin. Acet; Lot. Acid. Boric; Mangan. Butyras; Paraffinum, No. 7; Potassii Permanganas; Ung. Acid. Salicyl. 50%; Ung. Rusc. Co; Ung. Zinci Carboli.

**Baker's Dermatitis.**—All minor cracks, abrasions, etc., should be at once treated with Iodum or Argenti Nitras. Metchnikoff's Ointment most satisfactory, applied freely, rubbed in, and covered to exclude air. Evacuation of the vesicles hastens healing.

**Dhobie's Itch.**—Rub areas with a 10% solution of Chrysarobinum in equal parts of Acetone and Spiritus Methylatus Industrialis. In the evening wash off and use an Ung. Ac. Benz. (5%) et Ac. Salicyl. (3%). Next day reapply the Chrysarobinum. Ung. Resorcin. et Acid. Salicyl. (Castellani) is popular. Dhobie's Itch Ointment (Deeks) for itch and pruritus ani—Acidum Salicylicum 20 gr., Hydrargyrum Ammoniatum 20 gr., Bismuthi Subnitras 1 dr., Oleum Eucalypti 1 dr., Adeps Lanæ to 1 oz. Relapses with the Itch Ointment prevented by a powder of  $\frac{1}{2}$  oz. Sodii Bicarbonas in 8 oz. Talcum Purificatum.

**Diabetes Insipidus.**—Extractum Pituitarii Liquidum injection or nasal spray; Hypnotics; Thyroideum, Vasopressin.

**Diabetes Mellitus.**—Insulinum; Protamine Insulinate.

**Diaphoretics.**—Acidum Acetylsalicylicum, Aconitum; Alcohol; Ammonii Acetas, Ammonii Chloridum, Ammonii Citras, Antimonii et Potassii Tartaras, Antimonii Trioxidum, Apomorphinæ Hydrochloridum, Camphora; Ipecacuanha, Opium; Physostigmina; Pilocarpina, Potassii Citras, Pulvis Ipecacuanhæ et Opii, Quininæ Disalicylosalicylas, Salicin, Sodii Salicylas, Sp. Æther. Nitros.

**Diarrhoea.**—Acetanin, Acid Sulph. Aromat., Acid Sulph. Dil., Argenti Nitras, Bala; Berberina, Bismuthi Carbonas, Bismuthi Naphtholas, Bismuthi Salicylas, Bismuthi Tannas; Bismuthi Tribromphenas, Carbo, Catechu, Cinnamomum, Coto, Cotoina, Creta, Cupri Sulphas, Granati Fructus Cortex, Guaiacolis Valerianas, Guarana, Hæmatoxylinum, Ipecacuanha, Kaolinum, Kino, Krameria, Liq. Calc. Hydrox., Liq. Ferr. Acet., Liq. Ferr. Perchlor., Liq. Hydrogenii Peroxid., Liq. Sod. Chlorid. (by injection), Liq. Thymol. Co., Magnesii Peroxidum, Methylthioninæ Chloridum, Morphina, Naphthalenum, Oleum Ricini, Opium, Plumbi Acetas, Rheum, Salol, Serum Antidysentericum, Tinct. Chlorof. et Morph., Zinci Sulphas. Raw apple treatment (see Acidum Malicum).

**Digestives.**—Diastasum, Extractum Malti, Pancreatinum, Papainum, Pepsinum.

**Diphtheria.** (*Treatment*)—Antitoxinum Diphthericum (*Prophylaxis*)—Toxinum Diphthericum Detoxicatum. *Local*—Acidum Lacticum, Argenti Nitras, Garg. Chlor., Liq. Adrenal. Hydrochlor., Liq. Calc. Chlorinat., Liq. Chlori; Liquor Formaldehydi, Liq. Sod. Chlorinat., Neb. Ferr. Perchlor., Papainum, Pig. Menthol. et Toluen.; Resorcinol, Viola Crystallina.

**Dipsomania.**—Arseni Trioxidum, Atropinæ Sulphas, Ammonii Bromidum, Ammonii Carbonas, Capsicum, Chloralis Hydras, Cinchona, Colloidal Gold, Nux. Vomica, Potassii Bromidum, Sodii Bromidum, Strychninæ Hydrochloridum.

**Disinfectants.**—Acidum Sulphurosum; Aluminii Chloridum, Bromum, Calci Peroxidum; Calx Chlorinata, Carbo, Chromii Trioxidum, Cresol, Dettol and similar solutions, Hydrargyri Perchloridum, Liquor Formaldehydi, Liquor Hydrogenii Peroxidum, Paraformaldehydum, Phenol, Potassii Permanganas; Sulphur Sublimatum (burnt). See also Antiseptics.

**Disseminated Sclerosis.**—See Sclerosis, Disseminated.

**Diuretics (Saline).**—Ammonii Acetas; Ammonii Chloridum, Ammonii Citras, Ammonii Phosphas, Lithii Carbonas, Lithii Chloridum, Lithii Citras, Potassii Acetas, Potassii Bicarbonas, Potassii Citras, Potassii Nitras, Potassii Tartaras; Potassii Tartaras Acidus, Sodii Acetas, Sodii Benzoas, Sodii Citras, Sodii Formas.

(*Kidney Irritants*)—Agropyrum, Buchu, Copaiba; Cubeba, Guaiaci Resina, Kava; Oleum Juniperi; Oleum Santali, Oleum Terebinthinæ; Scoparium, Uva Ursi.

(*Cardiac*)—Convallaria; Digitalis; Scilla; Strophanthus.

(*Purine derivatives*).—Caffeina, Theobromina; Theobromina et Sodii Salicylas; Theophyllina et Sodii Acetas.

(*Mercurial*).—Hydrargyri Subchloridum, Hydrargyrum.  
(*Intravenous injection*).—Dextrosum; Injectio Mersalyli, Sodii Bicarbonas, Sodii Carbonas; Sodii Chloridum.

**Dropsy, Hepatic.**—Ammonii Chloridum, Cambogia, Hydrargyri Subchloridum, Jalapæ Resina, Oleum Juniperi, Scammoniae Resina

**Dupuytren's Contraction.**—Inj Thiosinam et Sod Salicyl, Inj Thiosinam et Phenazon, Thiosinam et Æthyl. Iodid, Thyroideum, Ung Acid. Salicyl

**Dusting Powders.**—Acidum Boricum, Agropyrum, Amylum, Iodoformum, Talcum Purificatum; Zinci Carbonas, Zinci Oleostearas, Zinci Oxidum

**Dysentery (Amœbic).**—Acetarsol, Emetina, Emetinæ et Bismuthi Iodidum; Emetinæ Hydrochloridum; Emetinæ Periodidum, Holarrhena, Ipecacuanha, Kurchi Bismuthi Iodidum. (*Bacillary*).—Serum Antidysentericum

**Dysmenorrhœa.**—Apiol, Cannabis; Castoreum, Cimicifuga, Cotarnina, Gelsemium; Gossypii Cortex, Ovarian hormones, Phenazonum, Piscidia, Potassii Bromidum, Pulsatilla, Sanguinaria, Valeriana, Viburnum *See also Analgesics.*

**Dyspepsia.**—Acid Hydrochlor Dil, Acid Hydrocyan Dil, Ammonii Carbonas, Bismuthi Carbonas, Bismuthi Subnitrates, Calci Peroxidum, Calumba, Capsicum, Carbo, Cardamomum, Ceru Oxalas, Chirata, Condurango, Creosotum, Diastase, Extractum Malti, Ferrum Redactum, Gentiana, Magnesium Carbonas Levis, Magnesium Carbonas Ponderosus, Nux Vomica, Pancreatinum, Papainum, Pepsinum; Phenol, Potassii Dichromas, Quassia, Rheum, Sodii Bicarbonas, Sodii Phenolsulphonas, Sp. Armor Co., Strychnina, Zingiber

**Dyspnœa.**—Æther (internally), Alcohol, Ammonii Carbonas; Amylis Nitris (by inhalation), Erythrityls Tetranitrates Dilutus, Liquor Ammoniac (by inhalation); Liquor Glycerylis Trinitratis, Sodii Nitris, Strychnina

**Earache.**—Oleat Atrop., Oleat Cocain, Oleat Morph, Oleum Amygdalæ, Oleum Olivæ, Phenol, Tinct Opi

**Ecbolics.**—Ergot preparations, Capsicum, Helleborus, Helonias, Lead salts, Oleum Pulegii, Pituitarium, Sabina, all drastic purgatives

**Eclampsia.**—Amylis Nitris; Choralis Hydras, Liquor Glycerylis Trinitratis, Mag Sulph (by injection), Morphina, Papaverina, Parathyroideum, Sodii Acetas, injections  $\frac{1}{2}$  drachm to the pint, Sodii Bicarbonas, 250 ml 3% solution intravenously repeated 3 hours later, Tab Erythrityl Tetranit *Routine Treatment*—Purgatives, e.g., Jalapa, Hydrargyri Subchloridum, Magnesium Sulphas, Oleum Crotonis *Diaphoretic*—Pilocarpina (of great value). *Nerve Sedatives*—Bromides, Tinct Chlorof et Morph

**Eczema.** *Internal*—Arseni Trioxidum, Calci Lactas, Ferri Salts, Ichthammol, Lac Coactum; Sodii Arsenas Anhydrosus, Sulphur

*Local*—Acidum Boricum, Acidum Pyrogalicum Oxidatum, Acidum Salicylicum, Argenti Nitras, Betanaphthol, Bismuthi Subnitrates, Calamina, Calci Iodas, Cocaina, Creosotum; Glycer Amyli, Hydrargyri Oxidum Rubrum, Hydrargyri Subchloridum, Hydrargyrum Ammoniatum, Ichthammol, Liquor Formaldehydi, Liquor Hydrogenii Peroxidi, Lot Trinitrophen, Oleum Cadinum, Oleum Chaulmoogræ, Oleum Olivæ (to remove incrustations), Oleum Picis, Oleum Rusci, Phenol, Pix Carbonis, Pix Liquida, Plumb Cerat, Plumbi Oleas; Plumbi Subacetates, Potassa Sulphurata, Potassii Carbonas (in a lotion), Pyrogallol, Resorcinol; Sodii Bicarbonas, Sodii Carbonas (in a lotion), Zinci Oleostearas, Zinci Oxidum, Zinci Peroxidum, Zinci Stearas

**Electric Current Injuries.**—*See Vol II*

**Elephantiasis.**—Sodii Aminarsonas.

**Emetics.**—Alumen, Antimonii et Potassii Tartras, Apomorphinæ Hydrochloridum, Cupri Sulphas; Emetinæ Hydrochloridum, Ipecacuanha; Sinapis, Sodii Chloridum, Zinci Sulphas

**Emmenagogues.**—(Estrinum, Pituitarium (Anterior Sex Hormone) (*Drastic Purgatives*) Aloe, Jalapa, Oleum Ricini (*Irritants*) Apiol, Oleum Petroselin, Oleum Pulegii, Oleum Rutæ, Oleum Sabinæ, Potassii Permanganas, Sabina. (*Stimulants of uterine muscle*) Caulophyllum, Ergota, Gossypii Cortex, Quinina.

**Emollients.**—Adeps, Adeps Lanæ, Cera Alba, Cera Flava, Cetaceum, Glycerinum; Oleum Amygdalæ, Oleum Arachis, Oleum Cocos, Oleum Gossypii, Oleum Olivæ, Oleum Sesami, Paraffinum Liquidum, Paraffinum Molle.

**Empysemæ.**—Iodides and iodine preparations. If patient too stout add thyroid to the iodine. If excess of lime in the blood, Sodii Citras or Potassii Citras. Keep bowels open with Sodii Sulphas

**Empyema.**—Liquor Hydrogenii Peroxidi for washing the pleura Douching with Liq. Sod. Chlorinat Chir, Vaccinum Pneumococcicum, Vaccinum Streptococcicum.

**Encephalitis Lethargica.**—Belladonna; Hyoscina; Sodii Salicylas

**Endocarditis.**—Acidum Nucleicum and Serum Antistreptococcicum and Vaccinum Antistreptococcicum, Belladonna, Caffeina, Cerevisiæ Fermentum, Digitalis; Extractum Pituitarii Liquidum, Ferri Perchloridum, Sodii Cacodylas, Vaccinum Pneumococcicum, Veratrum Local—Emp Bellad Ice Bag.

**Enteritis.**—See Gastritis.

**Enuresis.**—Arseni Trioxidum, Atropina, Belladonna, Bromides, Buchu; Calci Phosphas; Camphoræ Monobromidum; Ephedrinæ, Hydrochloridum, Ext Ergot. Liq, Ferri Iodidum; Ferri Perchloridum, Hyoscina; Hydrargyri Subchloridum, Hyoscyamus with Sodii Bromidum; Liq Strych. Hydrochlor, Nux Vomica, Phenazonum; Potassii Citras; Rhus Aromatica, Rhus Toxicodendron; Thyroideum, Tinct Lycopod Belladonna, Hyoscyamus and Bromide may help for a time, or even cure.

Nocturnal incontinence in children Ext Ergot Liq 5 minims to a child of 5 years, with 2½ minims Ext Glycyrrh Liq. and a drop of Oleum Menthæ Piperitæ effectual in a fortnight. Worth trying.—A Patton, *Brit med J*, ii/1930, 981

Mustard and pepper taken by boys found responsible for nocturnal incontinence.—T. W. Rothwell, *Brit med J*, i/1931, 42. All drugs found useless Train the child to empty bladder during the day at increasing intervals — J. Pereira Gray, *Brit med. J*, ii/1930, 908.

**Epidermomycosis.**—See Mycotic Affections of the Skin.

**Epididymitis.**—Aconitum; Calci Chloridum intravenously, Iodides, Saline Purgatives, Vaccinum Gonococcicum, Vin Antim

**Local.**—Atropinæ Sulphas (½ gr) and hypodermically, Guaiacol, Ice, Oleum Iodisatum, Lin. Pot. Iod, Argent Colloid., Hydrarg Colloid, Ung Iod. Denig; Heat, with moisture, Ung Bellad and Ung Hydrarg

**Epilepsy.**—Ammonii Bromidum, Amylis Nitris, Arseni Bromidum, Arseni Trioxidum, Auri Bromidum; Borax, Calci Bromidum, Camphoræ Monobromidum; Liq Aur et Arsen. Brominat.; Liquor Glyceryli Trinitratis, Parathyroideum, Peptonum; Phenobarbitonum solubile; Pilocarpina, Potassii Bromidum; Sodii Arsenas Anhydrosus; Sodii Bromidum, Sodii Nitris, Strontii Bromidum, Syr Pot Brom. et Pilocarp.; Venene; Zinci Bromidum, Zinci Iodidum; Zinci Sulphas, Zinci Valerianas.

**Epistaxis.**—Acidum Tannicum, Adrenalina, Alumen Exsiccatum, Calci Chloridum; Tinct. Hydrast. (in lotions), Kino (in powder as an insufflation), Kino Eucalypti, Liq. Hamam, Liquor Hydrogenii Peroxidi

**Epithelioma.**—See Cancer and X-Rays and Radium Therapy, Vol. II

**Erysipelas.** Internal—Aconitum Amidopyrina, p-Aminobenzenesulphonamide, Belladonna; Prontosil; Quinina; Serum Antistreptococcicum (hypodermically); Liq Ferr Perchlor.

**Local.**—Acidum Sulphurosum, Acidum Trichloraceticum, Belladonna, Calamina; Iodum, Trinitrophenol

**Erythema.**—Aconitum, Anthemus, Calci Lactas, Febrifuge Salines, Salicinum; Salicylates; Salol, Sulphur, Trilactine.

**Local.**—Kaolinum and Lot. Papav or Ung Papav, Past Hamam, High-Frequency Current, Liq Plumb Subacet Dil., Paraffinum Molle, Pellanthum preparations, Ung. Plumb Oleat., Ung Zinc Oxid., Zinci Oxidum

**Erythroedema.**—Attention to diet and painting the gum with Chromii Trioxidum (1%) to prevent secondary infection, the main points Large doses of Atropina or Calci Lactas suggested.—J. S. Fowler, *Brit med J*, i/1925, 1078.

**Erythroedema Polyneuritis (Pink Disease)**—Vitamin B

**Espondia.**—Antimonii et Potassii Tartras

**Exophthalmic Goitre (Graves' Disease)**—Arseni Trioxidum; Calci Salts, Digitalis; Ergotaminæ Tarttras; Ferri Salts, Fucus; Iodum; e.g., as Liq Iod Aq. Pituitarium (Posterior Lobe), Quininæ Hydrobromidum; Quininæ Sulphas; Suprarenalum, Sodii Fluoridum; Sodii Phosphas, Thyroidectomised animals' serum

**Local.**—Acidum Sulphurosum; Liq. Iod Oleos., Ung. Iod Denig.

**Expectorants.**—Acidum Citricum; Ammonii Acetas, Ammonii Benzoas, Ammonii Carbonas; Ammonii Chloridum; Ammonii Citras; Anisum; Antimonii et Potassii Tarttras; Apomorphinæ Hydrochloridum; Balsamum Tolutanum; Benzoinum; Cocillana; Codeina; Glycyrrhiza; Ipecacuanha; Marrubium; Scilla,

Senega; Sodii Acetas, Sodii Benzoas; Terebenum, Terpin Hydras; Urginea.  
**Eye, to Contract Pupil.**—*See* Miotics.  
**Eye, to Dilate Pupil.**—*See* Mydriatics.

**Fainting.**—*See* Collapse.

**Fat, to Reduce.**—*See* Obesity.

**Favus.**—*See* Parasites, Vegetable, on Skin.

**Fetid Breath.**—*See* Breath, Fetid. **Perspiration.**—*See* Perspiration, Fetid. **Nasal Discharges.**—*See* Ozæna.

**Fever.**—*See* Antipyretics.

**Fibrosis, Chronic Subcutaneous.**—Diabetic Diet, Fucus, Thyrodeum, Massage

**Fibrositis.**—Acidum Acetylsalicylicum, Potassii Iodidum

**Local.**—Chloralis Hydras et Menthol, Pig Chloral et Camph Co *See* also Rheumatism.

Dover's Powder at night gives rest. Aspirin 15 grains 6-hourly relieves pain and is often specific. For chronic fibrositis, Lugol's solution 5 minims twice daily. Thyroid promotes better metabolism—E B Clayton and J L Livingston, *Lancet*, 1/1930, 1420.

**Filariasis.**—Antimonii et Potassii Tartras

**Fissures of Nipples.**—*See* Nipples, Cracked.

**Fistula in Ano (Tuberculous).** **Local.**—Bismuthi Subnitras injections, Cupri Sulphas Injections, Liqueur Hydrogenii Peroxid, Ol Iodoform. after operation, Potassii Permanganas (packing with), Zinci ions

**Flatulence.**—Æther, Armoracia, Asafetida, Bismuthi Carbonas, Camphora, Capsicum; Carbo, Cardamomum, Creosotum, Magnesii Carbonas Levis, Magnesii Carbonas Ponderosus, Magnesii Oxidum Leve; Magnesii Oxidum Ponderosum, Oleum Juniperi, Oleum Lavandulæ, Oleum Menthæ Piperatæ, Phenol, Sodii Bicarbonas, Sodii Phenolsulphonas, Tinct Chlorof et Morph., Zingiber. *See* also Carminatives.

**Folliculitis, Pustular.**—Bismuthi Subchloridum, Ung Bism Subchlor

**Framboesia.**—*See* Yaws.

**Frost Bite.**—Friction with snow or cold water in a cold room best. Friction with Oleum Terebinthinæ and oil, or with spirit and Lin Sap. useful in early stages and after that the limbs should be raised on pillows and wrapped in cotton-wool. If blisters form, or discolouration, rub with Oleum Terebinthinæ, or with spirit containing 1 in 500 Hydrargyri Iodidum, or with Liq Iod—A W Mayo-Robson. Keep the parts cold, with foot raised slightly—smeared with some ointment, e.g., Lin. Calc Hydrox c Ol Lin, with 2% of Cocaine useful. Wrapping up causes pain—Lord Moynihan. Where there is moist gangrene, and especially where toxic absorption has taken place—amputation.—R H Jocelyn Swan. Counter-irritants relieve pain for a time, but do not materially affect speed of recovery—C Max Page

**Furunculosis.**—*See* Boils.

**Furunculosis Orientalis.**—*See* Oriental Sore.

**Gangrene.**—Amylis Nitrus, Liqueur Glycerylis Trinitratis, Quinina Hydrochloridum, Sodii Nitrus. **Local.**—Acidum Nitricum, Acriflavina, Creosotum, Inj Iod (vagina), Liqueur Hydrogenii Peroxid, Phenol, Saline injection (vulva)

**Gas Gangrene.**—Antitoxinum Vibriosepticum, Antitoxinum Edematis, Antitoxinum Welchicum.

**Gastralgia.**—Acidum Hydrocyanicum Dilutum, Alkalis, Belladonna, Bismuthi et Cinchonidinæ Iodidum, Bismuthi Oleas; Bismuthi Salicylas, Bismuthi et Sodii Tartras, Bromides; Cannabis; Ceri Oxalas, Chlorbutol, Chloroformum; Codeina; Creosotum, Liq Calc. Hydrox; Liq. Chloromorph, Liqueur Glycerylis Trinitratis, Magnesii Oxidum Leve, Magnesii Oxidum Ponderosum; Manganii Dioxidum Præcipitatum; Menthol; Mist Mag. Hydrox, Pepsinum; Zingiber.

**Local.**—Lin Sinap; Ung Ipecac et Croton

**Gastric Secretion, to diminish.**—Atropine, small dose in large volume of water on empty stomach

**Gastric Ulcer.**—*See* Ulcers, Gastric.

**Gastritis.**—Acidum Hydrocyanicum Dilutum, Bismuthi Carbonas; Bismuthi Salicylas; Papainum; Potassii Bicarbonas, Sodii Bicarbonas.

**Giddiness.**—*See* Vertigo.

**Gingivitis.**—*See* Gums, Inflamed, also Vincent's Angina.

**Glanders.**—Arsphenamina; Mallein; Mercurial Inunctions

**Glandular Enlargements.** *Internal*—Calcii Chloridum, Ferri Iodidum, Oleum Morrhuæ, Potassii Iodidum, Sodii Iodidum; Syr Iodotann.

*Local*—Hydrargyri preparations, Iodum, Plumbi Iodidum; Potassii Iodidum, X-Rays.

**Glaucoma.**—Physostigmia, Pilocarpina

**Gleet.**—See **Gonorrhœa**.

**Glossitis.**—Hydrargyri Perchloridum in Lotion (2 grains to 8 ounces).

**Glycosuria.**—See **Diabetes**.

**Goitre.** *Internal*—Ammonii Fluoridum; Arseni Trioxidum, Betanaphthol; Hydrargyri Iodidum Rubrum, Potassii Iodidum, Sodii Iodidum, Sodii Phosphas; Thymol, Thymus, Thyroideum

*External*—Liq Iod Fort, Ung Potass Iod

**Gonorrhœa.** *Internal*—Buchu, Conf. Piper, Copaiba, Cubeba, Ext Salix Nig Liq; Guaiacolis Cinnamas, Hexamina; Kava; Lithii Benzoes, Matica, Methylthioninæ Chloridum, Oleum Santali; Pareira, Potassii Bicarbonas, Salol; Vaccinum Gonococcicum

*Local*—Acriflavinum; Alumen, Aluminii Naphtholsulphonas; Argenti Citras, Argenti Nitras, Bismuthi Subnitras, Bismuthi Subiodidum, Bugin Bism et Plumb, Bugin. Iodof et Bellad, Bugin Iodof et Eucalyp, Bugin Iodof et Morph., Potassii Permanganas, Zinci Acetas, Zinci Chloridum, Zinci Permanganas, Zinci Phenolsulphonas, Zinci Sulphanilas, Zinci Sulphas

**Gout.** *Internal*—Acidum Acetylsalicylicum, Acidum Benzoicum, Acidum Quinicum; Acidum Thymicum, Antimonium Sulphuratum, Asparaginum, Caffeinæ Iodidum, Caffeinæ Salicylas, Cinchophenum, Colchici Cornus, Colchicina; Guaiaci Resina, Hexamina, Lithii Carbonas, Lithii Salts, Magnesii Oxidum Leve, Magnesii Oxidum Ponderosum; Neocinchophenum, Phenocolli Hydrochloridum, Piperazina, Piperidina, Potassii Acetas, Potassii Bicarbonas, Potassii Chloridum (as a table salt), Potassii Citras, Quininæ Salicylas, Sodii Bicarbonas, Sodii et Potassii Tartras, Sodii Phosphas, Sulphur

*Local*—Bain Alk, Bain Sod Chlorid, Lin Croton; Lithii Carbonas, Sodii Carbonas Exsiccatus (as a bath-salt)

**Granular Eyelids.**—See **Ophthalmia Tarsi**.

**Granuloma Inguinale.**—Antimonii et Potassii Tartras

**Graves' Disease.**—See **Exophthalmic Goitre**.

**Griping, to prevent.**—Atropina, Belladonna, Hyoscyamus, Oleum Anisi, Oleum Anthemidis; Oleum Cari, Oleum Caryophylli, Oleum Coriandri, Oleum Fœniculi; Oleum Menthæ Piperitæ, Oleum Menthæ Viridis, Oleum Myristicæ, Zingiber.

**Gums, Inflamed or Spongy.**—Alumen, Liquor Hydrogenii Peroxidi, Liq Iod Mit, Liq Salol Co, Liq Thymol Co, Lot Phenol et Borac, Potassii Chloras, Sodii Chloras, Tab Formaldehyd, Tinct Myrrh, Tinct Myrrh et Borac.

**Hæmatemesis.**—Acid. Sulph Aromat, Acid Sulph Dil; Acidum Tannicum, Adrenalina; Alumen, Alumen Ferricum, Liq. Ferr Perchlor, Morphina, Tinct. Ferr Perchlor, Pil. Plumb c Opio, Plumbi Acetas, Tab Plumb c Opio

**Hæmatinics.** (*In macrocytic anæmias*)—Extractum Hepatis Liquidum, Extractum Hepatis Siccum, Ventriculus Desiccatus. (*In microcytic anæmias*)—Arseni Trioxidum, Cupri Sulphas, Ferri Cacodylas, Ferri Carbonas Saccharatus; Ferri et Ammonii Citro-arsenis, Ferri et Mangani Citras, Ferri et Quininæ Citras, Ferri Iodidum, Ferri Phosphas Saccharatus, Ferri Quininæ et Strychninæ Citras, Ferri Sulphas, Ferrum Redactum, Hæmoglobinum, Mangani Chloridum, Mangani Glycerophosphas, Mangani Hypophosphus, Mangani Peroxidum, Medulla Rubra, Sodii Cacodylas

**Hæmoptysis.**—Amylis Nitris (by inhalation), Calcii Chloridum (rectally); Congo Red; Moccasin venom (by injection), Morphina, Oxygenium (by injection),

**Hæmophilia.**—Calcii Chloridum, Calcii Lactas, Magnesii Chloridum, Magnesii Lactas.

*Local*—Acidum Tannicum, Calcii Chloridum, Ferri Perchloridum, Hamamelis, Russell's viper venom

**Hæmorrhage.**—See **Hæmatemesis**; **Hæmoptysis**; **Hæmorrhage, Uterine**.

**Hæmorrhage, Uterine.** *Internal*—Cotarnina, Ergota; Ergotoxina; Hydrastina, Hydrastinina, Hydrastis, Moccasin venom (by injection), Ovarian hormones

**Local**—Liq Adrenal Hydrochlor; Russell's viper venom

**Hæmorrhoids.** *Internal*—Cascara Sagrada, Conf Piper., Conf. Senn.; Conf. Senn. et Sulphur.; Conf Sulphur, Pulv. Glycyrrh Co, Sennæ Folium, Sulphur Sublimatum

**Local**—Ext. Kramer Sicc (in a suppository); Ferri Sulphas (as an ointment), Liq. Plumb. Subacet. Fort (in a lotion), Liq Hamam (as a lotion), Phenol and Ext. Hamam Liq. (injection), Phenol in oil (injection), Plumbi Acetas; Supp. Acid Tannic.; Supp. Adrenal., Supp. Bism Subgall, Supp. Hamam et Zinc. Oxid; Supp. Iodoform., Tinct. Hamam (in a lotion), Ung. Acid Tann; Ung. Adrenal.; Ung. Adrenal. et Cocain.; Ung. Cocain.; Ung. Conu, Ung. Eucalyp; Ung. Gall.; Ung. Gall. c. Opto, Ung Hamam, Ung. Plumb. Acet, Ung Supraren.; Zinci Oxidum.

**Hæmostatics.** (*Internal Hæmorrhage*)—Acid Sulph Aromat; Adrenalina; Calci Chloridum; Calci Lactas; Catechu, Cotarninæ Chloridum; Cotarninæ Phthalas; Emetina; Ephedrina; Ergota; Ergotoxina, Ergotoxinæ Æthanosulphonas, Ergotoxinæ Phosphas; Extractum Pituitarii Liquidum; Gelatinum, Hydrastina; Hydrastina; Hydrastis, Moccasin venom (by injection); Plumbi Acetas, Serum Normale; Sodii Citras.

(*External Hæmorrhage*).—Acidum Tannicum, Adrenalina, Alumen, Cotarninæ Chloridum; Cotarninæ Phthalas, Cupri Sulphas; Ferri Perchloridum, Galla, Hamamelidis Cortex; Hamamelis, Hydrastina Hydrochloridum, Hydrastis, Kino; Krameria; Liquor Hydrogenii Peroxidi, Moccasin venom (injection), Oleum Terebinthinæ; Russell's viper venom; Serum Normale

**Hair, to Promote Growth of.**—Hæmoglobinum and Tonics, Medulla Rubra *See also* **Seborrhœa.**

**Local.**—Amylis Nitris; Cantharis, Hydrargyri Perchloridum (in spirit lotion), Pilocarpina (lotion), Resorcinol (lotion)

**Hair, to Remove.**—Thallii Acetas has been given internally for epilation in ringworm.

**Local.**—Baryta Sulphurata, Calx Sulphurata; Pigmentum Thymolis, Sodii Sulphidum 25 to 40% Aqueous Solution, X-Rays and Electric Needle, *see* VII

**Hair-washes.**—Lot. Plumb. et Sulphur., Lot Quinin., Lot Staphisag, Sp Piment. Co.; Sp. Resorcin.

**Halitosis.**—*See* **Breath, Fetid.**

**Hay Fever.** *Internal*—Belladonna; Camphora, Euphorbia, Grindelia, Potassii Iodidum, Quinina

**Local**—Hay Fever vaccine, Insuff Bism et Morph, Insuff Menthol, Insuff Menthol et Cocain.; Liq Adrenal. Hydrochlor, Liquor Hydrogenii Peroxidi; Neb. Adrenal Aromat; Neb. Adrenal et Cocain, Neb Adrenal et Ephed, Neb Benzoin Co; Neb Benzoin Co c. Cocain et Quinin, Neb Cocain Co; Neb Ephedrin Co; Neb Eucalyp Co, Neb Menthol et Thymol. Co.; Peptone injections, Fig. Menthol. et Toluén. (to nasal mucous membrane), Quininæ Hydrochloridum (in a spray or nasal douche).

**Headache, Nervous.**—Acetanilidum, Acidum Acetylsalicylicum, Acidum Hydrobromicum Dilutum and Bromides, Amidopyrina, Ammonii Valerianas, Caffeina; Caffeina Valerianas; Guarana; Kola, Phenacetinum, Phenazonum; Phenylurethanum; Quinina.

**Headache, Post-concussional.**—4 to 8 ounces 50% Magnesi Sulphas *per rectum*.—A. Fielsing, *Brit med. J.*, ii/1930, 907.

**Headache (due to high blood pressure)**—Antimonii et Potassii Tartras, Cannabis; Pil. Hydrarg. *See also* **Blood Pressure, to Reduce.**

**Heart.**—*See* **Cardiac Tonics and Dropsy, Cardiac, also Vasodilators.**

**Hepatic Colic.**—*See* **Calculi, Biliary.**

**Hepatitis.**—Emetina.

**Herpes Zoster.**—Arsenic, *e.g.*, Liq Arsen.; Inj. Morph. (hypodermically for pain), Quininæ preparations; Salines and Saline Aperients, General Tonics

**Local.**—Bismuthi Oleas; Cocaine preparations; Colloid Simp.; Colloid Anodyn.; Crem. Zinc. preparations; Hydrargyrum Ammoniatum; Ichthammol, Lin. Calc. Hydrox. c. Ol. Lini (or mixed with Ung. Zinc Oxid 3:1); Liquor Hydrogenii Peroxidi; Lot. Calamin.; Neoarsphenamina; Fig. Menthol. (for pain), Quinine Iodisation; Ung. Hydrarg. Oleat; Ung. Menthol. (for pain), Ung. Zinc. Oleat.; Ung. Zinc. Oxid.

**Hiccough.**—Alcohol Benzylicum for persistent; Amylis Nitris; Camphora, Carbonei Dioxidum; Chloralis Hydras; Ext. Ergot Liq.; Liq. Adrenal. Hydrochlor, Liq. Ammon. Acet Dil; Lobelina; Morphine preparations; Moschus;

Oleum Succini, Pilocarpinæ Hydrochloridum, Sodii Bicarbonas, Spt. Æther; Spt. Chlorof., Tinct. Capsic; Tinct. Valerian. Simp

**Hodgkin's Disease.**—See **Lymphadenoma**.

**Hook-worm.**—See **Ankylostomiasis** and **Anthelmintics**.

**Hydrarthrosis.** *Local.*—Cataplasma Salicyl. Co., Ung. Hydrarg. Co. See also **Edema**.

**Hydrocele.**—Iodine and Phenol Paint; Iodum injected; Morestin's Fluid; Sodii Morrhuas.

**Hydrophobia.**—Immediate use of actual or electric cautery or Acidum Nitricum, Argenti Nitras (solid) or other caustic paste at hand. Antirabic Vaccine.

**Hyperchlorhydria.**—Alkalis, Alumin. Hydrox.; Belladonna; Bismuthi Carbonas and Pancreatium, Bismuthi et Sodii Tartras, Cerni Oxalas; Kaolinum; Magnesii Carbonas Levis; Magnesi Trisilicas; Nux Vomica (large doses), Oleum Olivæ; Pepsinum.

**Hyperhidrosis.**—See **Perspiration, Excessive**.

**Hyperpleisia and Hyperpleisia.**—See also **Vasodilators; Blood Pressure, to Reduce; Cardiac Tonics, and Dropsy, Cardiac**.

**Hypertrichosis.**—See **Hair, to Remove**.

**Hypnotics.** (*Non-analgesic*)—Alcohol, Allobarbitonum, Barbitonum; Barbitonum Solubile; Carbromalum, Chloralformamidum, Chloralis Hydras; Methylosulphonal; Phenobarbitonum, Phenobarbitonum Solubile; Sulphonal.

(*Analgesic*)—Butylchloralis Hydras, Codeina, Codeinæ Phosphas; Diamorphinæ Hydrochloridum, Hyoscina Hydrobromidum; Hyoscyaminæ Hydrobromidum, Morphina (and salts); Opium, Papaveretum; Paraldehydum, Urethanum.

**Hysteria.**—Acidum Hydrobromicum Dilutum (and bromides); Ammonii Carbonas; Ammonii Valerianas; Asafoetida, Bornylis Valerianas, Caffeinæ Valerianas; Camphoræ Monobromidum; Cannabis, Ferri Valerianas; Moschus; Nux Vomica, Quininæ Valerianas, Sodii Valerianas, Strychnina; Sumbul; Valeriana; Zinci Valerianas.

**Ileus, Acute.**—An emetic. Acetylcholine Hydrochloride; Choline Chloride, Extractum Pituitarum Liquidum; Sod. Tauroglycocholas, Physostigmina, Prostigmin; Saline intravenously.

Human bile *per rectum* 2 ounces in 4 ounces saline every 4 hours. Hypertonic saline (a quart of 3%) intravenously also useful. Gas-Gangrene Antitoxin suggested prophylactically prior to operation. See also **Constipation**.

**Impetigo.**—Remove crusts with Oleum Olivæ or by Cataplasma Amyli et Acid. Boric., then 10% Ung. Hydrarg. Ammon., Acriflavina, Liq. Calc. Chlorinat. c. Acid. Boric., Ung. Virid. Nit.; and see **Eczema**.

**Impotence.**—Arseni Trioxidum; Cannabis; Cantharis; Damiana; Ferri Perchloridum; Formates; Glycerophosphates, Nux Vomica, Phosphorus, Piperazina; Sanguinaria; Strychnina, Syr. Ferr. Phosph. c. Quinin. et Strych., Testicular Hormones and Extracts, Yohimbina; Zinci Phosphidum.

**Incontinence of Semen.**—Arseni Trioxidum, Belladonna; Bromides, Camphoræ Monobromidum; Chloralis Hydras, Ergota, Ferri Perchloridum, Ferri Phosphas; Hyoscina; Hyoscyamina, Phenazonum; Salix Nigra, Syr. Ferr. Phosph. c. Quinin. et Strych.

**Incontinence of Urine.**—See **Enuresis**.

**Indigestion.**—See **Dyspepsia**.

**Inebriety.**—See **Dipsomania**.

**Inflammation.**—Acetanilidum; Aconitina; Aconitum; Antimonium; Belladonna; Digitalis; Gelsemium; Hydrargyri Subchloridum, et cum Opio; Opium, Phenazonum; Quinina; Salicin, Veratrina.

*Local.*—Cataplasma. Kaolin; Cataplasma. Salicyl. Co.; Glycer. Plumb. Subacet., Hirudo; Iodum; Pasta Magnesii Sulphatis.

**Influenza.**—Acidum Acetylsalicylicum; Aconitum, Belladonna; Calcii Naphtholsulphonas; Camphora; Influenza vaccine; Liq. Ammon. Acet. Dil.; Neb. Cocain. Co.; Neb. Eucalypt. Co.; Oleum Cinnamomi; Oleum Eucalypti; Phenazonum, Phenazon. c. Caffein. Efferv.; Phenazoni Salicylas; Phenocollum Hydrochloridum; Pulv. Ipecac. et Opi; Potassii Bicarbonas; Quinina; Salicinum, Sodii Salicylas, Sp. Æther. Nitros.; Sp. Ammon. Aromat.; Sp. Cinnam., Symmetrical Urea compounds; Vap. Eucalypt. Co.; Vap. Ol. Pini.

For an ordinary severe case give Acidum Acetylsalicylicum and Pulv. Ipecac. et Opii aa. 10 grains, after customary aperient, and repeat in 6 to 8 hours; follow by a simple diaphoretic. For *headache*, Phenacetinum 5 grains with

**Caffeina** 2 grains. For *foul tongue*, Sodii Bicarbonas and Sodii Phenolsulphonas. For *vomiting*, reduce feeds and give Liq. Iod. Mit. 1 minim hourly for 6 doses. For *cough*, Syr. Cocillan. Co.; Syr. Codein. Phosph., or Elix. Diamorph. et Terpin. For *sleeplessness*, Bromide or Paraldehydum.

The following formula was useful in the 1918 epidemic:—Quininæ Hydrochloridum, Camphoræ Monobromidum, Hexamina, aa. 2 grains, Methylthioninæ Chloridum 1 grain in one capsule, one at onset followed by another in 4 hours; not more than 4 in 24 hours—most cases require but 3. Camphora a valuable drug given as follows—Camphora  $\frac{1}{2}$  grain, Quininæ Hydrochloridum 3 grains, Acidum Acetylsalicylicum 5 grains. Two powders daily.

**Insect Bites.**—See Bites and Stings, also Parasites and Pediculosis.

**Insomnia.**—See Hypnotics.

**Intertrigo.** *Local.*—Acidum Boricum; Bismuthi Carbonas, Calci Carbonas, Camphora, Crem. Zinc. preparations, Ichthammol diluted with 50 parts Aqua, Iodum Colloid, Kaolinum, Liq. Calc. Hydrox., Liq. Iod. Mit. diluted with 3 times volume of Sp. Colon; Liq. Pic. Carbon. diluted with equal volume of Sp. Colon, Methylthioninæ Chloridum, Paraffinum Mollé, Talcum Purificatum, Ung. Acid. Boric., Ung. Rub. Scarlat., Ung. Thorii Oxid., Ung. Zinc. Oxid., Zinci Oleostearas, Zinci Salicylas.

**Intestinal Antiseptics.**—See Antiseptics.

**Intestinal Obstruction.**—See Ileus.

**Intestinal Worms.**—See Anthelmintics.

**Iodism.**—Acidum Sulphanilicum, Preparations containing Ammonia.

**Iritis.**—Colchici Cormus, Colchici Semen; Hydrargyri Perchloridum, Hydrargyri Subchloridum, Iodum; Oleum Betulæ, Potassii Iodidum, Pilocarpina, Calci Acetylsalicylicum, intravenously.

*Local.*—Belladonna; Duboisinæ Sulphas, Gutt. Atrop.; Lamell. Atrop. Scopolamina.

**Itch.**—See Scabies.

**Jaundice.**—Acid. Nitro-hydrochlor. Dil.; Aloe; Ammonii Chloridum, Benzozates; Calci Chloridum; Cinchophenum (of new-born), Elix. Gent. Acid.; Ext. Euyoni, Ext. Irid., Ferri Succinas, Hydrargyri Subchloridum, Hydrarg. c. Cret.; Hydrastis; Iodoformum; Mangani Sulphas, Mist. Senn. Co.; Pilocarpina, Podophylli Resina, Salol, Sodii Phosphas, Sod. Phosph. Efferv., Taraxacum. Contramine for Arspenamine jaundice. To relieve skin irritation dilute Acid. Nitric. Lotion or Sol. Sod. Bicarb., Lic. Pic. Carbon; Past. Hamam., Ung. Rusc. Co.

**Kala Azar.**—Organic arsenic compounds *q.v.*, Antimonii Oxidum, Antimonii et Potassii Tartaras or Antimonii et Sodii Tartaras; Organic antimony compounds, Fournéau "309", Bayer "205."

**Keloid.**—Inj. Thiosinamin. et Sod. Sal., Radium, Thiosinamin. et Æthyl Iodid.; X-Rays.

**Laryngeal Ulcers.** *Local.*—Acidum Lacticum, also Quininæ Dihydrochloridum, as pigment and nebula.

**Laryngismus Stridulus.**—Aconitum, Amyli Nitris, Belladonna, Bromides, Chloralis Hydras; Coniunæ Hydrobromidum, Emetina, Gelsennium, Piscidia.

**Laryngitis.**—Aconitum, Ammonii Bromidum, Antimonii et Potassii Tartaras, Codeina, Diamorphinæ Hydrochloridum, Hydrargyri Subchloridum, Mist. Glycyrrh. Co.

*Sprays and Inhalations.*—Neb. Eucalypt. et Pini, Neb. Menthol. Co., Vap. Ammon. Chlorid., Vap. Benzoin., Vap. Ol. Pini.

*Local.*—Lin. Capsic., Lin. Capsic. Co. applied on flannel over the larynx.

**Laxatives.**—See Cathartics.

**Leishmania Affections.**—See Kala Azar.

**Leprosy.**—Acid. Trichloracetic, Ephedrina, Oleum Chaulmoogra, Oleum Hydnocarp; Oleum Hydnocarp. Æthylicum, Potassii Iodid.; Sodii Chaulmoogra, Sodii Morrhuas.

**Leucocythæmia.**—Arsenical preparations; Benzenum; Ferri Salts; Glycero-phosphates; Iodum; Marrubium, Phosphorus, Syr. Iodotann.; Syr. Iodotann. c. Phosph., X-Rays.

**Leucorrhœa.**—See Tonics.

*Local.*—Acetarsol, Acidum Boricum, Acidum Tannicum; Alumen; Bismuthi Carbonas; Dec. Gall.; Dec. Granat. Fruct. Cort. et Dec. Querc. (as injections); Hydrargyri Iodidum Rubrum; Hydrargyri Perchloridum; Hydrastis; Inf. Kramer. Conc.; Pessus Quinin. Hydrochlor.; Pinus Canadensis (in lotions);



Potassii Permanganas; Tinct. Laric.; Zinci Chloridum, Zinci Phenolsulphonas and Zinci Sulphas (as injections).

**Leukæmia.**—See *Leucocythæmia*.

**Leukoplakia.**—Radium.

**Lice, to Kill.**—See *Parasiticides*.

**Lichen.** *Internal.*—Arseni Trioxidum, Ferri Cacodylas, Liq Hydrarg. Perchlor; Magnesii Cacodylas; Sodii Arsenas Anhydrosus; Sodii Cacodylas  
*Local*—Acidum Hydrocyanicum Dilutum (in a lotion for application to the skin), Ichthammol; Inj Bismuthi Salicyl.; Ol. Cadinum.

**Liver Abscess.**—See *Abscess, Liver*.

**Locomotor Ataxia.**—Alumini Chloridum; Amylis Nitris; Arsphenamina; Cannabis, Chloralformamidum, Ergota, Hexamina; Hydrargyri Benzoas, Hyoscina; Inj. Acid Nuclei, Mercury inunctions, Morphina, Neoarsphenamina, Oleum Iodisatum, Oleum Morrhuæ; Phenacetinum, Phenazonum; Potassii Bromidum, Potassii Iodidum, Quinina, Salvarsanised, Serum Sodii Bromidum, intrathecal injection; Sodii Cacodylas; Sodii Salicylas; Strychnina (with acid), Tryparsamidum.

**Lubricators for Catheters.**—Ol. Lubric, Paraff. Carbol, Past. Trag Co, Parenol.

**Lumbago.**—Acidum Acetylsalicylicum, Ammonii Chloridum, Belladonna, Camphoræ Monobromidum, Cunicifuga, Colchici Cornus; Colchici Semen, Conf. Guaiac. Co; Morphina; Potassii Iodidum; Quinina; Sodii Iodidum, Sodii Salicylas; Tinct Guaiac. Ammon.

*Local.*—Collod. Anodyn, Collod. Atrop, Collod. Bellad.; Emp. Bellad Vir, Emp. Capsic.; Emp. Menthol.; Emp. Pic, Gossyp Capsic, Lin. Ammon, Lin. Bellad.; Lin. Capsic, Lin. Menthol; Lin. Methyl. Sal; Lin. Opi Ammon, Methylis Chloridum (applied on cotton-wool), Methylis Salicylas, Oleum Betule; Parogen. Menthol; Tinct. Capsic Fort; Ung Methyl. Salicyl. Co.

**Lupus.**—Acidum Nucleicum injection, Arseni Trioxidum; Bismuthi injections and *per os*; Cacodylates, Hydrargyri Iodidum Rubrum, Inj Sod Morrhuæ, Iodum; Oleum Chaulmoogra, Oleum Morrhuæ, Phosphorus; Quininæ preparations; Salicinum; Thyroideum.

*Local.*—Acidum Cinnamicum; Æthylis Chloridum; Arsphenamina; Auri Chloridum; Bismuthi Oxyiodogallas; "Brass Paste" and preparations; Camph. Salicyl.; Cupri Oleas; Emp. Pyrogall.; Finsen light, Hydrargyri Nitras; Inj Thiosinam. et Phenazon.; Iodoformum, Liqueur Hydrogenii Peroxidi; Oleum Chaulmoogra preparations; Past. Zinc. Oxid. c. Acid. Salicyl; Potassii Permanganas; Resorcinol; Sodii Morrhuas; Thiosinamina; Thymolis Iodidum, Tuberculinum; Ung Acid. Salicyl (50%), Ung. Pyrogall.; Zinci Chloridum, Zinc and other Iodisation.

**Lupus Erythematosus.**—Arsenicals; Quinina.

*Local.*—Auri Chloridum injections; Auri et Pot. Cyanid injections, Auri et Sodii Thiosulphas injections; Carbonei Dioxidum (solid), Finsen lamp; Hydrargyri Iodidum Rubrum; Phenol, Ung. Bism. Subchlor., Ung. Thorii Oleat.

**Lymphadenoma.**—Arseni Trioxidum; Coley's Fluid; Mangan. Colloid, X-Rays.

**Lymphangitis.**—Mangani Butyras, Glycerinum Ichthammolis

**Malaria.**—Acidum Salicylicum; Arseni Trioxidum, Atebrin, Atebrin-musonate, Berberinæ Sulphas, Cinchonidinæ Sulphas; Cinchoninæ Hydrochloridum; Ferri et Ammonii Citro-Arsenis; Methylthioninæ Hydrochloridum, Phenocoll Hydrochloridum; Phloridzinum; Piperina; Plasmouquine Simplex, Quinetum, Quinidina; Quinina; Quininæ Bisulphas (by injection), Quininæ Dihydrobromidum (by injection); Quininæ Dihydrochloridum (by injection); Quininæ Hydrochloridum; Quininæ Sulphas; Quino-Plasmoquine; Salicinum; Sodii Arsenas Anhydrosus; Sodii Salicylas; Totaquina.

**Malarial Coma.**—Inj. Quinin. et Urethan. intravenously *q.v.* **Relapsing Fever.**—Bismuthi et Sodii Tartas.

**Malignant Pustule.**—See *Anthrax*.

**Malignant Tumours.**—See *Cancer*.

**Malta Fever.**—See *Undulant Fever*.

**Mammary Abscess.**—See *Breast, Inflammation of*.

**Mango Toe.**—Castellani's Paint.

**Mania.**—Ammonii Bromidum; Apomorphina; Barbitonum; Cannabis; Chloralis Hydras; Coniina Hydrobromidum; Diamorphina; Hyoscina; Hyoscyamina; Methylsulphonal; Morphina; Opium; Paraldehydum; Potassii Bromidum; Sodii Bromidum; Sulphonal.

**Marasmus.**—Arsenical preparations; Conf. Glycerophosph Co, etc., Elix. Hæmoglob.; Emuls. Ol. Morr. c. Ovolecithin.; Ext. Medull. Rub.; Ferri preparations, Meat preparations, Ovolecithinum; Vitamin D preparations

**Mastitis.**—See **Breast, Inflammation of.**

**Measles.**—Acidum Nucleicum injections; Aconitum, Adult serum, Amido-pyrin; Ammonii Carbonas, Calx Sulphurata, Cinnamomum Pulverata for prophylaxis (German measles); Ipecacuanha, Liq. Ammon. Acet. Dil., Placental Extract; Potassii Tartaras Acidus; Sp. Æther Nitros; Tinct. Bellad., Acidum Acetylsalicylicum, Phenacetinum, and Pulv. Ipecac. et Opii combined

**Melancholia.**—Bromides; Camphora; Cannabinæ Tannas, Cannabis, Damiana; Elix. Gent. Acid, Elix. Ovolecithin., Moschus; Nux. Vomica; Oleum Elliott, Opium, Phosphorus, Pil. Potentin Co., Sodii Taurglycocholas; Syr. Glycerophosph Co.; Tinct. Opii Valerianates

**Menière's Disease.**—Acidum Salicylicum, Bromides, Caffeina, Gelsemium, Pelletierina.

**Meningitis, Cerebrospinal.**—Antimeningo. Serum; Belladonna, Hexamina, Hydrargyri Subchloridum, Iodides, Opium, Veratrum, Lumbar puncture Mercurial injections

**Menopause.**—Caulophyllum, Hydrastis, Ovarian hormones and Corpus Luteum, Viburnum

The whole train of instability of the endocrine glands is set going by the ovarian insufficiency upsetting the mental as well as the physical balance, leading to gloominess, apprehensiveness and irritability. Corpus Luteum is beneficial, especially for flushing and other vasomotor disorders—the dose advised by the makers is often too small. Thyroid when signs of myxœdema. Even mild hyperthyroid symptoms excitability, tachycardia, flushing and loss of weight, are definite contraindications. Rest, bromides, belladonna, quinine hydrochloride are to be used to hyperthyroidal states.—G. Riddoch, *Brit. med. J.*, ii/1930, 987

**Menorrhagia.**—Acidum Scleroticum; Acid. Sulph. Dil., Alumen Ferricum, Amylia Nitris, Berberinæ Sulphas, Bromides, Calci Chloridum, Cannabinæ Tannas, Corpus Luteum; Cotarninæ Phthalas, Digitalis Folium, Elix. Ergot. c. Ferr., Elix. Ovolecithin.; Ergota, Oleum Erigeron, Erodium Cicutarium; Ferri Perchloridum, Hamamelis (see note *infra*), Hydrastis, Liq. Ferr. Subsulph.; Mist. Senecio Co.; Ovarian preparations, Plumbi Acetas, Sodii Citras, Thyroideum; Viburnum, Zinc Ions.

**Migraine.**—Dextrosum; Ergotaminæ Tartaras, Nitroglycerinum

**Milk, to Check Secretion.**—Acidum Agaricum, Atropinæ Sulphas, Belladonna

**Local.**—Collod. Atrop.; Collod. Bellad.; Emp. Bellad., Emp. Bellad. Vir., Glycer. Atrop., Glycer. Bellad.

**Milk, to Increase Flow of.**—Anterior Pituitary (lactogenic principle), Alcohol, Cotton-seed extract; Edestine, Jaborandi, Pilocarpina, Tyronormin.

**Miotics.**—Physostigmina; Pilocarpina

**Moles.**—Carbonei Dioxidum (solid), Electrolysis, Liq. Sod. Æthylat

**Morphine Habit.**—Æthylmorphinæ Hydrochloridum, Autoserotherapy, Berberina, Camphora, Codeina in "withdrawal"; Colloidal Gold, Emetina, Hyoscina, Mist. Bellad.; Nux. Vomica, Pilocarpin. Nit., Quinina, Sodii Bromidum, Sparteinæ Sulphas, Strychnina, Xanthoxylum

**Mosquitoes, to ward off.**—See **Bites and Stings.**

**Mumps.**—See **Parotitis.**

**Myalgia (Muscular Rheumatism)**—Acidum Acetylsalicylicum, Ammonii Chloridum; Calci Lactas, Cimicifuga, Cinchophenum; Ferri Salts, Ibogaina, Inj. Atrop. hypodermically, Inj. Morph., Potassii Iodidum; Salicylates, Syr. Calc. Chlorid

**Local.**—Emp. Capsic.; Glycer. Bellad.; Lin. Bellad.; Lin. Camph.; Lin. Camph. Co.; Lin. Capsic.; Menthol; Methylis Acetylsalicylas, Oleum Caryophylli, Parogen. Iod., Ung. Methyl. Sal. Co.; Ung. Veratrin.

**Myasthenia Gravis.**—Electricity, Ephedrina, Glycine, Physostigmina, Potassii Chloridum; Prostigmin.

**Fungal Affections of Skin.**—Æthylis Iodidum inhalation; Castellani's Magenta Paint, Lintum Acidi Borici, Mycozol; Phenylmercuric Nitrate; Sodii Perboras; Succus Limonis; Ung. Acid. Salicyl.

**Mydriatics.**—Atropina; Atropinæ Sulphas; Belladonna; Cocaina; Cocainæ Hydrochloridum; Duboisinæ Sulphas; Ephedrina; Ephedrinæ Hydrochloridum, Homatropinæ Hydrobromidum; Hyoscina; Hyoscinae Hydrobromidum.

**Myxœdema.**—Thyroideum.

**Nævi.** *Local*.—Acidum Nitricum; Carboni Dioxidum (solid); Chromi Trioxidum; Collod. Simp; Liq. Sod. Æthylat.; Zinci Chloridum; Zinci Iodidum; Zinci Nitras.; High-frequency Current.

**Narcotics.**—See Hypnotics.

**Nasal Catarrh.**—See Catarrh, Nasal.

**Nephritis.**—Aconitum; Agropyrum; Alkalis; Buchu, Calci Chloridum, Copaiba; Digitalis with Caffeina; Erythrityls Tetranitras Dilutus, Dec. Hordei, Hydrastis; Neptal; Oleum Santali; Potassii Citras; Potassii Nitris; Potassii Iodidum; Potus. Imperial.; Pulv. Pot. Nitras. Co.; Salt-free diet; Scoparium; Sodii Salicylas; Strophanthus; Theobrominæ Acetylsalicylas; Theophyllina, Thyroideum; Urea; Uva Ursi; Saline solution injected may prolong life.

**Alkaline Salts**—Ammonii, Potassii and Sodii Acetas, Tartras, Citras and Bicarbonas probably act on the renal epithelium. The slight excess of saline constituents thus produced in the blood stimulates the renal epithelium to excrete them. They draw with them a certain amount of water, and the flow is increased. *Cardiac Tones*—Digitalis acts directly on heart muscle and arteries and increases flow of urine by quickening flow of the blood through the kidney—especially useful where blood pressure is low or the heart failing before resistance too high for it. Caffeina, Theobromina and allied drugs—these stimulate both heart and renal cells. Theobromina et Sodii Salicylas is more potent than Caffeina. Where condition of the kidneys is the main cause, begin with alkaline salts—Herringham. *Acute nephritis in childhood*.—Diuretics are probably harmful and should never be used. In uræmia, Magnesii Sulphas intravenously is of undoubted value.—L. G. Parsons, *Brit. med. J.*, ii/1926, 367.

**Interstitial nephritis.**—Generous milk diet, green vegetables and fresh fruits, restrict animal proteins and limit carbohydrate intake. Prohibit artificially-sweetened puddings, etc.—W. E. Deeks, *Diet and Disease*, 1927.

**Ischaemic nephritis** (due to arterial degeneration) and toxic nephritis (an inflammatory reaction to bacterial or other toxins) described.—D. S. Russell, *Lancet*, i/1930, 204.

**Chronic parenchymatous nephritis with œdema**, but without much evidence of Nitrogen retention—large doses of alkali resulted in clearing up the œdema.—A. A. Osman, *Brit. med. J.*, i/1930, 337.

**Chronic nephritis**—Value of alkalis in. To be used except in rare instances where a preliminary estimation has shown a decrease in the plasma bicarbonate. May be useful for promotion of diuresis.—A. A. Osman, *Lancet*, ii/1930, 945.

The urine should be kept alkaline by giving basic ash foods, i.e., milk and vegetables (with reasonable variety of meat, fish and eggs) together with adequate alkaline salts.—D. M. Lyon, D. M. Dunlop and C. P. Stewart, *Lancet*, ii/1931, 1013.

**Nephrosis.**—A group of cases of nephritis with œdema with good prognosis, treated logically with diets rich in protein, and thyroid. There is enormous loss of albumin in cases of this type.—T. Izod Bennett, *Lancet*, i/1931, 115.

*S. aureus* and other organisms suggested as cause of nephrosis.—L. C. Bruce, *Lancet*, i/1931, 268.

**Nervous Debility, Nervousness.**—See Neurasthenia.

**Neuralgia.**—Acetanilidum, Acidum Acetylsalicylicum, Acidum Hydrobromicum Dilutum and Bromides, Aconitum; Amidopyrina; Ammonii Chloridum, Belladonna, Butylchloralis Hydras, Caffeina, Cannabis, Cimicifuga, Conium, Gelsemium; Methylacetanilidum, Phenacetinum; Phenazonum, Phosphorus; Piscidia; Quinina; Sodii Arsenas Anhydrosus; Sodii Salicylas.

*Local*.—Aconitina; Æthylis Bromidum (in a liniment); Æthylis Chloridum, Alcohol (local injections); Atropina, Belladonna, Capsicum, Chloral Camph.; Chloroformum; Cocaina, Collod. Gossyp. Capsic.; Guaiacol (as a paint); Lin. Aconit.; Lin. Croton.; Liq. Epispast. (painted over painful nerve); Menthol, Methylis Chloridum (applied on cotton wool), Methylis Salicylas; Oleum Caryophylli (with Oleum Olivæ); Ung. Methyl Salicyl. Co.; Veratrina.

**Neurasthenia.**—Acid. Phosph. Dil.; Acidum Hydrobromicum Dilutum and Bromides; Ammonii Valerianas; Arseni Trioxidum; Calcii Glycerophosphas, Carbromalum; Damiana; Ferri Arsenas; Ferri Glycerophosphas, Ferri Valerianas; Hæmoglobinum; Liq. Aur. et Arsen. Brominat.; Lithu Glycerophosphas; Male hormones; Ovocelithinum; Phosphorus; Quinina; Sodii Arsenas Anhydrosus; Sodii Valerianas; Sumbul; Syr. Ferr. Phosph. c. Quinin. et Strych.; Valeriana; Yohimbina; Zinci Phosphidum; Zinci Valerianas.

**Neuritis.**—Acidum Acetylsalicylicum, Amidopyrina, Arseni Trioxidum; Iodides, Mercurials, Morphina; Phenacetinum, Phenazonum; Electricity.

**Local.**—Acidum Hydrochloricum

**Night Sweats.**—Acidum Agaricum; Acidum Camphoricum; Atropina; Belladonna; Guaiacolis Camphoras; Guaiacolis Carbonas; PicROTOXINUM, Zinci Oxidum.

**Nipples, Cracked.**—Collod. Aceton; Collod. Flex, Collod. Stypt; Glycer. Acid Tannic.; Glycer. Plumb. Subacet, Ung. Acid. Boric., Ung. Borac.; Ung. Cocain.

**Nipples, to Harden.**—Alcohol (diluted).

**Nits.**—See Parasitocides.

**Nocturnal Emissions.**—See Incontinence.

**Nose Bleeding.**—See Epistaxis.

**Nymphomania and Satyriasis.**—Bromides; Belladonna; Camphora, Conii Folium, Hyoscina, Stramonium.

**Nutrients.** *By the mouth*—Amygdala Dulcis, Casernum Solubile, Cetraria, Chondrus, Dextrosium; Extractum Malti, Ficus, Gelatinum, Ichthyocolia, Lactosum, Manna, Mel Depuratum; Mist. Sp. Vin. Gall.; Oleum Amygdalæ, Oleum Cocois; Oleum Morrhuæ, Oleum Olivæ, Peptonum, Peptonum Bovinum, Prunus, Succ. Bov.; Sucrosum. *By the rectum*—Dextrosium; Enema Nutr. Supp. Nutr.

**Obesity.**—Alkali Carbonates and Citrates, Ammonii Iodidum; Dinitrophenols; Fucus, Magnesii Sulphas, Potassii Iodidum; Saccharinum (instead of sugar); Soda Iodidum; Soda Sulphas; Thyroideum

**Odorants.**—Aq. Mel., Moschus, Oleum Auranti; Oleum Bergamottæ, Oleum Cedri; Oleum Gerani; Oleum Graminis Citrati, Oleum Lavandulæ, Oleum Neroli; Oleum Rosæ; Oleum Sassafras, Saflorum; Sp. Colon, Sp. Lavand. Terpineol; Terpinol; Tonca Semen.

**Oedema.**—Calcii Chloridum, Calcii Lactas (of feet), Calcii Gluconas; Injectio Mersalyli; Mercury preparations, Theophylline Ethylenediamine, Theophyllina et Sodii Acetas. See also Diuretics.

**Local.**—Cataplasma. Kaolin.; Cataplasma Salicyl. Co., Lin. Pot. Iod. c. Sap.; Magnesii Sulphas (solution), Ung. Hydrarg. Co (of ankles).

**Ophthalmia.**—See Conjunctivitis.

**Orchitis.**—Acetanilidum; Aconitum, Antimonial, Iodoprotein tablets, Potassii Iodidum; Saline aperients.

**Local.**—Emp. Hydrarg., Glycer. Bellad., Guaiacol, Liq. Iod. Mit., Magnesii Sulphas Solution, Ung. Bellad.; Ung. Iodi

**Oriental Sore.**—Berberina Sulphas Injection, Carboni Dioxidum (solid); Emetina, Inf. Emet.; Organic antimony and arsenic compounds, Ol. Phosphor.

**Osteomalacia.**—Calcii Salts, Ext. Parathyroid, Ol. Phosphor

**Osteomyelitis.**—Past. Bism. et Iodof

**Otitis and Otorrhœa.**—Acidum Salicylicum, Aconitum; Iodides; Saline Aperients.

**Local.**—Acidum Tannicum, Acriflavina; Bismuthi Tribromphenas, Calot's Solution; Chromii Trioxidum, Glucosum Liquidum (solution as swab), Gossyp. Iodof.; Glycerinum; Glyc. Ferr. Perchlor., Hydrargyri Subchloridum; Ichthammol, Insuff. Alumen.; Insuff. Iod. et Ac. Boric., Insuff. Iodof.; Liquor Hydrogenii Peroxidi; Liq. Iod. Mit., Liq. Picis Carbon, Mag. Sulph.; Mercurchromum; Oleum Terebinthinæ, Potassii Permanganas, Resorcinol; Thy-molis; Zinci Chloridum.

Potassii Iodidum 10 grains taken well diluted every 4 hours. Every 2 hours external meatus filled with Liquor Hydrogenii Peroxidi retained 10 minutes. Nascent iodine liberated in tissues of middle-ear cleft.—S. P. Sturm, *Brit. med. J.*, ii/1928, 1118.

**Otosclerosis.**—Parathyroideum

**Oxytocics.**—Extractum Pituitarii Liquidum; Oleum Ricini, Quinina (and Salts).

**Ozena.**—Acidum Boricum; Acidum Tannicum, Alumen; Aluminii Acetas, Aluminii Naphtholsulphonas; Glycer. Thymol. Co., Iodoformum; Iodum, Liquor Formaldehydi (in a pigment or spray), Liquor Hydrogenii Peroxidi; Liq. Sod. Chlorinat.; Liq. Thymol. Co.; Methylthioninæ Chloridum (in a lotion); Menthol; Potassii Permanganas; Paraffinum Liquidum; Ung. Hydrarg. Nit. Dil. (applied with a brush); Vap. Chlori; Zinci Sulphas.

**Pain, to Alleviate.**—See Analgesics.

**Pancreatitis.**—Pancreatinum

**Panniculitis.**—Acid Acetylsalicyl., Caffeina Citras; Amudopyrina and Magnesi Acetylsalicylas combined; Phenacetinum.

**Paralysis, Hemiplegia.**—Acetylcholina; Arsenicals, Ergota; Ferri Salts, Nux Vomica; Phosphorus; Physostigma; Serum Mercurial

**Paralysis, Paraplegia.**—Arsenic compounds (organic), Acetarsol, Ergota, Phosphorus; Physostigma, Serum Mercurial; Strychnina

**Paralysis Agitans.**—Atropina; Bulbocapnina, Hyoscina, Phenobarbitonum.

**Parasiticides.**—Acidum Benzoicum, Acidum Salicylicum, Balsamum Peruvianum, Benzenum; Cevadilla, Chlorbutol, Chrysarobinum, Derris; Hydrargyri Iodidum Rubrum, Hydrargyri Perchloridum; Hydrargyrum, Hydrargyrum Ammoniatum; Liquor Formaldehydi; Magenta; Oleum Sassafras; Pix Carbonis, Phenol; Potassa Sulphurata; Pyrethri Flos; Saffrolum; Sodii Sulphas; Staphisagria; Sulphur Sublimatum; Sulphuris Chloridum; Sulphuris Iodidum, Veratrinum

**Paratyphoid.**—See Typhoid.

**Parkinsonism, Post Encephalitic.**—Banisterina, Hyoscina Hydrobromidum, Nicotina injections; Stramonium; Tinct Bellad See also Encephalitis, Epidemic (Vol. II).

**Parotitis (Mumps).**—Aperients, Saline, Iodides; Phenazonum; Salicylates

**Local.**—Glycer Bellad. to neck; Iodum; Ung. Methyl Salicyl

**Pediculosis Capitis (Lousiness).**—See Parasiticides.

**Pericarditis.**—Acidum Nucleicum; Aconitum; Caffeina, Cerevisia Fermentum, Digitalis Folium; Hydrargyri preparations; Lot. Quass., Opiates and Musk (to relieve pain); Potassu Iodidum; Sodii Iodidum; Salicylates; Emp Bellad; Lin. Bellad; Hirudo; Ice, Blisters.

**Peritonitis.**—Acetanilidum; Aconitum; Antitoxinum Welchicum; Antitoxinum Œdematiens, Antitoxinum Vibriocephalicum; Colloidal Metals, Digitalis Folium; Hydrargyri Subchloridum cum Opio; Hyoscyamus; Opium and Belladonna; Phenazonum, Tuberculinum Pristinum; Veratrum Viride. *For collapse*—Camphor injections, Caffeina et Sodii Salicylas, etc.; Vaccines.

**Perspiration, Excessive.**—Acetylcholina; Acid. Agaricum; Acid. Phosph. Dil., Acid. Sulph. Aromat., Atropina and injections hypodermically, Atropina Methylbromidum, Belladonna; Ergota, Pilocarpina; Picrotoxinum, Quinina preparations; Acidum Tannicum; Betanaphthol sol in alcohol and glycerin., Chromii Trioxidum (of feet); Formosyl, Kaolinum, Past Zinci Oxid. Co.; Ung. Plumb. Oleat.; Zinci Boras; Zinci Carbonas; Zinci Oleostearas, Zinci Oxidum, "X" Rays. See Radiology, Vol. II.

**Perspiration, Fetid.**—Mineral and vegetable acids, Sulphur (of feet) and Tonics.

**Local.**—Acidum Salicylicum cum Talc.; Alumen, Borax, Lot Acet., Lot Phenol, Ung. Glycer Plumb Subacet.; Ung. Phenol; Ung. Plumb. Oleat.; Ung. Sulphur; Zinc et Kaolin (of feet), Zinci Oleostearas cum Thymol.

**Pertussis.**—See Whooping Cough.

**Pharyngitis.**—See Throat, Inflammation.

**Phlebitis.**—Warm compresses, and rest the limb with it raised. Potassii Citras, Hexamina with Sodii Salicylas and Ammonii Benzoas—E C McCarthy Morris.

**Phosphaturia.**—Sodii Phosphas Acidus and general tonic treatment.

**Phthisis.**—Acidum Cacodylicum and Cacodylates; Acidum Camphoricum, Acidum Cinnamicum, Acidum Hydrocyanicum; Acidum Hydrofluoricum (in an inhalation); Acidum Nucleicum; Allium; Allylis Sulphidum; Artificial Pneumothorax; Auri et Sodii Thiosulphas; Calcii Hypophosphis; Creosotum, Creosoti Carbonas; Eugenol, Ferri Hypophosphis; Guaiacol (and compounds), Hydrargyri Succinidum, Iodoformum (intravenous); Jacobson's solution; Liquor Formaldehydi (in an inhalation); Magnesii Peroxidum (to arrest diarrhoea); Oleum Morrhuæ; Oleum Picis; Oleum Pini Pumilionis; Oleum Terebinthinæ; Oxygen (by injection), Piperidinæ Guaiacolas; Pix Liquida; Potassu Guaiacolsulphonas; Quinina Hydroxidum; Quinina Hypophosphis; Salol; Sodii Cinnamas (by injection); Sodii Fluoridum; Sodii Hypophosphis; Sodii Oleas, Terebentum; Terpin Hydras; Tuberculinum Pristinum; Urea; Vaccinum Tuberculinum; Vap. Chlor.; Vap. Iod. Ether.; Zinci Oxidum

**Piles.**—See Hæmorrhoids.

**Pityriasis. Local.**—Glycer Borac.; Hydrargyrum Oleatum; Oleum Cadinum; Sp. Resorcin., Ung. Chrysarob.; Ung. Chaulmoog.; Ung. Glycer. Plumb. Subacet.; Ung. Pic Carbon.

**Plague.**—Iodum (intravenously), Serum Antipestis, Vaccinum Bubonicum  
**Pleurisy.**—Aconitum, Ammonii Acetas, Ammonii Carbonas, Antimonii et Potassii Tartaras, Apocynum, Bryonia, Pilocarpinæ Nitras, Potassii Iodidum, Sodii Iodidum, Sodii Salicylas

**Local.**—Cataplasma Kaolini; Cataplasma Sinap, Chart Sinap; Emp Bellad. Gossyp. Capsic; Liq. Epispast (painted on chest), Lin Sinap, Liq Iod Fort

**Pleurodynia.**—*See Myalgia.*

**Pneumonia.**—Aconitum, Æthylhydrocupreina, Amidopyrina, Ammonii Carbonas, Ammonii Acetas, Antimonii et Potassii Tartaras; Belladonna; Digitalis Folium, Enema Terebinth (flatus); Felton's serum, Ferri Acetas; Hyoscyamus, Ipecacuanha; Moschus, Oxygenium, Potassii Citras, Quinin. Dihydrochloridum, Salicinum, Serum Antipneumococcicum I and II, Sodii Salicylas; Strophanthus, Symmetrical Ureas, Thyroid and Manganese, Vaccinum Pneumococcicum.

**External.**—Cataplasma Kaolini, Cataplasma Sinap; Chart Sinap; Gossyp Capsic, Hirudo, Lin Sinap

**Poisons.**—*See Antidotes* under each heading in the text.

**Polypl.** **Local.**—Liquor Hydrogenii Peroxidi, Styptics

**Polyuria.**—To reduce output—Ext. Pituitarii Liq. *See also Incontinence.*

**Port-wine Stains.**—Electrolysis, Ultra-violet Light,

**Post-Partum Hæmorrhage.**—*See Hæmorrhage.*

**Pregnancy.**—*See Uterus, to contract.*

**Pregnancy, Vomiting of.**—Acidum Hydrocyanicum Dilutum, Aconitum, Adrenalina, Argenti Nitras; Arseni Trioxidum, Belladonna, Calcii Gluconas, Cerui Oxalas; Chloralis Hydras, Chlorbutol, Chloroformum, Cocaina, Corpus Luteum, Creosotum, Dextrosum; Iodides, Liq Iod Mit (1 m in 1 oz of water every 2 hours), Menthol, Mist. Bism et Pancreatin, Morphine preparations, Nux Vomica, Pepsinum, Phenazonum; Potassii Permanganas, Quinina, Sp Nucus Jugland.

**Prickly Heat.**—Lot Hydrarg Perchlor (q v) made with Acid Hydrochlor Dil.

**Prolapsus Uteri.**—Quinine injected

**Prostration.**—Amylis Nitris, Catha and Coca preparations, Oxygenium (inhalation), Stimulants *See also Collapse.*

**Prurigo.**—Arseni Trioxidum, Bromides, Cantharis, Ferri salts, Pilocarpina, Quinina, Sodii Carbonas

**Local.**—Alcohol Isopropylicum, Borax, Cocaina, Ichthammol, Iodum Colloid, Liq. Ammon Dil., Liq. Hydrarg Perchlor, Liq Plumb Subacet Dil, Lot Phenol, Pig Chloral. et Camph Co; Pilocarpina, Staphisagria, Pix Liquida, Ung. Bism Oleat., Ung Phenol; Ung Rusc. Co, Ung Sulphur

**Pruritus Ani, Vulvæ, etc.**—A B A, Acidum Sulphurosum; Acidum Tannicum, Aloe; Argenti Nitras in Sp Æther Nitros, B A B A N, Bismuthi Carbonas, Calcii Lactas, Chlorbutol, Ext Hydrast Liq and Ext. Hamam. Liq, injected; Hydrargyrum Oleatum and with Morphina, Hydrargyri Subchloridum dusted on, Lot Alk., Lot Alumen; Lot Hydrarg Nig, Lot Pic Carbon Alk., Lot. Phenol, Lot Phenol et Cocain; Menthol and Borax (in a lotion), Orthocaina, Past. Pic Carbon. Æther-Soluble, Potassii Cyanidum (in a lotion), Sodii Salicylas, Sodii Silicas; Sodii Thiosulphas, Supp Betanaph, Supp Ichtham, Tinct Cannab; Trinitrophenol, Ung Acid Boric, Ung Acid Salicyl, Ung Betanaph Co, Ung. Chlorof; Ung Cocain, Ung Conii, Ung Gall. c Opio, Ung Glycer Plumb Subacet., Ung Phenol, Ung Rusc Co, Uranu Oleas, Ultra-Violet Light; X-rays

**Psoriasis.**—Acidum Cadodicum, Anthrarobinum, Betanaphthol, Enesol, Ferri Arsenas, Ferri Cacodylas, Ichthammol, Liquor Arsenicalis; Pil Asiaticæ, Salicinum, Sodii Arsenas Anhydrosus; Sodii Cacodylas, Thyroideum

**Local.**—Acid Pyrogall Oxid, Acidum Salicylicum, Chrysarobinum, Cignolin, Creosotum, Hydrargyri Nitras, Hydrargyri Subchloridum; Ichthammol, Liq Plumb. Subacet Dil.; Phenol, Pyrogallol, Oleum Cadnum, Oleum Chaulmoogræ, Oleum Olivæ (to remove incrustations), Oleum Rusci; Phenol, Pix Carbonis; Potassa Sulphurata, Resorcinol; Sapo Mollis (to remove incrustations), Thymol; Ung Sulphur; Ung. Sulphur. Hypochlor, X-Rays.

**Ptyalism.**—*See Salivation.*

**Puerperal Fever.**—Acetanilidum; Acriflavina (injection); *p*-Aminobenzene-sulphonamide, Antitoxinum Scarlatinum, Calcii Phosphas (*per os*); Calcium Sulphide, Carbo Animalis (intravenously); Ferri Perchloridum, Iodum (intravenously), Jaborandi; Liquor Glycerylis Trinitratus; Mercurochromum, intravenously; Oleum Terebinthinæ; Opium; Phenazonum; Pilocarpina; Potassii Bromidum combined with Belladonna; Proctoöl Quinina (2 grains every 4

hours); Rivanol, intravenously, Saline transfusion, Sodii Nucleas, Sulpharsphenamina, Symmetrical Ureas, Vaccinum Streptococcicum; Vitamin A.

**Purgatives.**—*See Cathartics.*

**Purpura.**—Acidum Ascorbicum; Calciu Chloridum; Ergota, Extractum Hepatis, Ferri Salts; Phosphorus; Quininæ preparations; Oleum Terebinthinæ.

**Purpura Hemorrhagica.**—Blood transfusion; Moccasin venom (by injection).

**Pyæmia.**—Autogenous vaccine.

**Pyelitis.**—Acidum Mandelicum; Acriflavina; Benzoates, Collinsonia, Hexammina; Camphoras; Hexyl-Resorcinol, Ketogenic Diet (*see* Vol II); Oleum Erigeronis; Potassu Citras; Pyridium; Salol, Vaccin B coli

*Local*—Argent Colloid, Mercurochromum

**Pyloric Stenosis.**—Atropina; Atropinæ Methylnitrates

**Pyorrhæa.** *Local*—Liq Arsen, Liq Hydrogen Peroxid; Sodii Ricinoleas, Tinct Ipecac, Zinci Permanganas

**Pyrosis.**—Acid Hydrocyan Dil, Bismuthi Carbonas; Bismuthi Subnitrates, Carbo, Ceru Oxalas, Magnesi Oxidum Leve, Magnesi Oxidum Ponderosum, Magnesi Carbonas Levis, Magnesi Carbonas Ponderosus, Sodii Bicarbonas, Sodii Naphtholsulphonas

**Quinsy.**—*See Throat, Inflamed.*

**Rabies.**—*See Hydrophobia.*

**Rat-bite Fever.**—Neoarsphenamina

**Raynaud's Syndrome.**—Acetylcholina; Electrotherapy, Protein Therapy

**Relapsing Fever.**—Neoarsphenamina, Sodii Arsanilas *See also Malaria.*

**Remittent Fever.**—*See Malaria.*

**Restoratives.**—*See Collapse and Fainting.*

**Rheumatic Endocarditis.**—*See Endocarditis.*

**Rheumatism, Acute.**—Acetanilidum, Acidum Acetylsalicylicum; Aconitum, Caffeinæ Iodidum; Caffeinæ Salicylas; Calciu Naphtholsulphonas; Cimicifuga; Colchici Cormus, Gelsemium, Guaiacol, Methylis Salicylas, Neocinchophenum, Oleum Betulæ, Opium, Phenazoni Salicylas; Phenocolli Hydrochloridum, Potassu Acetas; Potassu Bicarbonas, Potassu Chloridum (as a table salt); Potassu Citras; Quininæ Salicylas, Salicinum, Salol; Sodii Bicarbonas, Sodii Iodas (by subcutaneous injection); Sodii Salicylas; Strontii Salicylas.

*Local*—Lin. Methyl. Salicyl Co.; Oleinat Aconit., Oleum Betulæ; Ung Aconitum; Ung Methyl. Salicyl, Ung. Methyl. Salicyl. Co.

**Rheumatism, Chronic.**—Acidum Acetylsalicylicum; Acidum Hydriodicum Dilutum and Iodides, Amidopyrina, Calcium Ortho-iodoxybenzoate, Cimicifuga; Cinchophenum; Electrotherapy; Gelsemium; Gold compounds; Guaiaci Resina, Iodine Ionisation, Lithii Carbonas, Lithii Citras, Lithii Iodidum; Lithii Salicylas; Magnesi Oxidum Leve; Magnesi Oxidum Ponderosum, Magnesi Carbonas Levis; Magnesi Carbonas Ponderosus; Neocinchophenum, Oleum Cajuputi, Oleum Crotonis, Oleum Sulphuris, Phenacetinum; Phenocolli Hydrochloridum; Phytolacca, Piperazina; Quininæ Dihydriodidum; Quininæ Hydriodidum; Salol; Sodii Bicarbonas, Sodii Formas, Sodii Iodas (by subcutaneous injection); Sodii Salicylas, Streptococcus Rheumaticus Vaccine, Strontii Salicylas, Sulphur Sublimatum; Thyroideum.

*Local*—Acidum Formicum; Aconitum preparations; Atropina; Bee venom, Belladonna; Borneol; Capsicum; Camphora; Chloralis Hydras; Chloroformum, Electrotherapy; Gossyp. Capsici; Guaiacol; Histaminæ Phosphas Acidus, Menthol; Methylis Salicylas; Oleum Betulæ; Oleum Cajuputi, Oleum Chaulmoogra; Oleum Crotonis; Oleum Eucalypti; Oleum Pini Pumilionis; Oleum Sassafras; Oleum Sinapis Expressum; Oleum Succini; Oleum Terebinthinæ; Oleum Thymi; Opium; Sodii Carbonas Exsiccatus (as a bath-salt); Sodii Chloridum; Ultra-Violet light; Ung. Methyl. Salicyl. Co.

**Rheumatoid Arthritis.**—Acidum Acetylsalicylicum; Calcium Ortho-iodoxybenzoate; Cinchophenum, Colchici Cormus; Colchici Semen; Gold compounds; Guaiacol; Guaiacolis Carbonas; Guaiaci Resina; Lac Coactum, Lithii Carbonas; Lithii Citras; Lithii Guaiacas; Lithii Iodidum; Neocinchophenum; Oleum Morrhuæ; Phenocolli Hydrochloridum; Piperazina; Potassu Iodidum; Protein Therapy; Sodii Iodidum; Streptococcus Rheumaticus Vaccine; Thiosinamin. et Æthyl. Iodid., Thyroideum.

**Rhinitis.**—*See Catarrh, Nasal.*

**Rickets.**—Acid. Phosph. Dil.; Calciferol, Calcii Hypophosphus; Calcii Lactas, Calcii Lactophosphas; Calcii Phosphas, Cinchona preparations; Eliz. Ovocleithin.; Emuls. Ol. Morrhu. c. Glycerophosph.; Ext. Malt. Liq. c. Hæmoglob.; Ferri Hypophosphus; Ferri Phosphas; Glycer Glycerophosph c Medull. Rub.;

Liq. Calciterol., Liq. Calc Hydrox., Liq. Ferr. Hypophosph., Liq. Ferr. Pepton. c. Mang.; Medulla Rubra; Ovocleithrum, Oleum Morrhuæ; Ol. Phosphor.; Phosphorus; Sodii Phosphas; Sulphur Sublimatum; Syr Calc. Chlorid.; Syr. Calc. Hypophosph.; Syr. Calc. Lactophosph.; Syr. Calc. Lactophosph. c. Ferr.; Syr. Ferr. Iod., Thyroideum, Ultra-Violet Light, Vitamin D concentrates

**Ringworm.**—Thalli Acetas *Local*.—Acidum Benzoicum; Acidum Salicylicum; Acidum Sulphurosum; Chrysarobinum, Cupri Oleas, Hydrargyri Iodidum Rubrum; Hydrargyrum Ammoniatum, Hydrargyrum Oleatum, Iodum; Liq. Ferr. Perchlor. Fort.; Liquor Formaldehydi, Liq. Hydrarg. Nit. Acid., Oleum Picis; Phenol, Phenylmercuric Nitrate; Pig. Trinitrophenol. et Camphoræ; Resorcinol; Sulphuris Iodidum; Thymol; Ung. Sodii Chloridi; Ung. Sulphur. Hypochlor.; X-Rays

**Rodent Ulcer.** *Local*.—Acidum Trichloraceticum, Chromii Trioxidum; Carbonei Dioxidum (solid), Radium, Rubrum Scarlatinum, X-Rays, Zinc Ions. **Rubefacients.**—*See Counter-Irritants.*

**Saint Vitus's Dance.**—*See Chorea.*

**Saliva, to Promote.**—Armoracia, Lobelia, Mercurials, Pelletierina; Phytostigma; Pilocarpina, Piper Nigrum, Potassii Iodidum; Sinapis, Tabacum; Tab. Formaldehyd.; Tinct. Pyreth.

**Saliva, to Check Excessive.**—Acid Hydrochlor. Dil.; Atropina, Belladonna; Chlorates, Coto, Picrotoxinum. Of syphilis after excessive Mercury. Sodii Chloras.

*Local*.—Acidum Boricum; Alumen; Borax, Chlorates, Creosoti Vapor.

**Scabies.** *Local*.—Acidum Sulphurosum, Balsamum Peruvianum; Betanaphthol, Hydrargyri Perchloridum; Hydrargyrum Ammoniatum, Liq. Calc. Sulphurat.; Mitigal, Naphthalenum; Potassa Sulphurata, Pyrethrum (ointment), Styraz; Sulphur Sublimatum, Sulphuris Iodidum; Ung. Potassii Polysulphidi; Ung. Sulphur. Hypochlor.

**Scalds.**—*See Burns.*

**Scarlet Fever (Treatment).**—Antitoxinum Scarlatinum. (*Prophylaxis*).—Toxinum Scarlatinum.

*Local.*—Garg. Chlor., Liquor Hydrogenii Peroxidi (in a gargle); Liq. Sod. Chlorinat. (in a gargle)

**Sciatica.**—Acetanilidum, Amidopyrina, Atropina, Calcii Naphtholsulphonas, Cimicifuga, Cinchophenum, Guaiacum, Lithii Citras, Lithii Guaiacas, Lithii Iodidum, Lithii Salicylas; Methylacetanilidum, Methylthionine Chloridum, Morphina, Neocinchophenum, Phenazonum, Piperazina; Potassii Iodidum, Sodii Iodidum, Sodii Salicylas

*Local*.—Acidum Osmicum (as 1% injection); Aconitum, Aconitina; Æthylis Chloridum, Alcohol (local injections), Belladonna, Capsicum, Chloroformum, Collod. Anodyn., Gossyp. Capsic., Menthol, Methylis Chloridum (with Æthylis Chloridum) (applied on cotton-wool), Methylis Salicylas, Oleum Betulæ, Opium, Quininæ et Ureæ Hydrochloridum

**Sclerosants.**—Dextrosum, Lithii Salicylas, Phenol; Quininæ et Ureæ Hydrochloridum; Quininæ Hydrochloridum (with Urethanum), Sodii Chloridum; Sodii Morrhuas, Sodii Salicylas.

**Sclerosis, Disseminated.**—Bulbocapnina; Ext. Hepatis, Parosan; Sodii Aminoarsonas; Sodii Cacodylas; Vaccinum Typho-Paratyphosum.

**Scurvy.**—Acidum Ascorbicum, Succus Aurantii; Succus Limonis; Vitamin C concentrates.

**Sea-Sickness.**—Acidum Hydrobromicum and Bromides; Amylis Nitris (by inhalation); Atropinæ Sulphas; Caffeina; Cerii Oxalas; Chloralformamidum, Chloralis Hydras, Chlorbutol; Cocainæ Hydrochloridum; Dextrosum; Hyoscyaninæ Hydrobromidum; Liquor Glycerylis Trinitratis; Sodii Nitris; Syntropan; Tinct. Ipecac.

**Seborrhœa.**—Resorcinol; Sapo Durus; Sapo Mollis; Ung. Acid. Salicyl., Ung. Hydrarg. Oxid. Rub.

**Sedatives.** *Gastric.*—Acidum Hydrocyanicum Dilutum; Ammonii Bromidum; Aqua Laurocerasi; Bismuthi Carbonas; Bismuthi Citras; Bismuthi et Ammonii Citras; Bismuthi Salicylas; Bismuthi Subnitras; Bismuthi Tannas, Carbonei Dioxidum (solution); Cerii Oxalas; Chloralformamidum; Chloralis Hydras; Chlorbutol; Chloroformum; Coca; Cocaina; Morphina; Opium, Papaveretum; Potassii Bicarbonas; Potassii Bromidum; Sodii Bicarbonas; Sodii Bromidum.

*Respiratory.*—Acidum Hydrobromicum Dilutum; Æther; Æthylmorphinæ



Hydrochloridum, Ammonii Bromidum; Amyli Nitris, Bromoformum; Chloralis Hydras, Chloroformum, Codeina, Codeinæ Phosphas, Diamorphinæ Hydrochloridum, Gelsemina, Gelsemium, Grindelia; Morphina (and salts), Opium; Papaveretum, Potassii Bromidum, Prunus Serotina; Sodii Bromidum, Sodii Nitras, Sp. Æther Nitros.

*Central nervous system*.—Acidum Acetylsalicylicum, Acidum Hydrobromicum Dilutum, Acidum Hydrocyanicum Dilutum, Ammonii Bromidum, Camphoræ Monobromidum; Gelsemina; Gelsemium; Hyoscine Hydrobromidum, Hyoscyaminæ Hydrobromidum, Lithii Bromidum; Morphina (and its salts), Opium, Phenacetinum, Phenazonum; Physostigminæ Sulphas, Potassii Bromidum, Sodii Bromidum. *See also Hypnotics.*

**Septicæmia and Pyæmia.**—Acidum Nucleicum, Acriflavina, Ferri Perchloridum, Hydrargyri Benzoas, Hydrargyri Perchloridum intravenously, Mercurochromum; Quinina, Resorcinol; Salicinum. Serum Antistreptococcicum; Saline injection, Sodii Cacodylas; Sulphites, Symmetrical Urea compounds, Thyroid and Manganese, Vaccinum Antistreptococcicum, Viola Crystallina, injection *See also Puerperal Fever.*

**Shingles.**—*See Herpes Zoster.*

**Shock, Surgical.**—Acacia in saline (or plain), Adrenalina, Caffeina et Sodii Salicylas; Calcii Gluconas, Camphora in Æther; Coramine; Dextrosium, Ergota, Liq. Sodii Chlorid. Physiol., Morphina, Oxygenium with Alcohol, Pituitarium, Spiritus Vini Gallici, Strychnina

**Salagogues.**—*See Saliva, to Promote.*

**Sickness.**—*See Vomiting, also Sea-sickness.*

**Skin.**—*See Eczema, Psoriasis, etc.*

**Skin Proliferants.**—Allantoinum, Rubrum Scarlatinum, Symphytum

**Skin Sterilisation.**—*See Antiseptics.*

**Sleeping-sickness.**—*See Trypanosomiasis.*

**Sleeplessness.**—*See Hypnotics.*

**Small-pox.**—Ext. Hepatis; Vaccinum Vaccinæ *See also Variola.*

**Snake-bite.**—Serum Antivenenosum *See also Vol. II*

**First Aid.**—Apply tourniquet a few inches above bite, and then give immediate subcutaneous injection of Serum Antivenenosum supplemented by incision and suction if the bite has been inflicted by a large snake, and symptoms are severe Repeat every half-hour Spray the part with Æthylis Chloridum whilst making incisions and rubbing in Potassii Permanganas Gelatin injection for hæmorrhage

Cocainæ Hydrochloridum injected in full doses at the site of puncture caused by fangs of the snake not only relieves pain, but causes reduction of the swelling if promptly used Well combined with Potassii Permanganas Oozing hæmorrhage is reduced by taking large quantities of gelatin solution *per os*

**Soporifics.**—*See Hypnotics.*

**Spasm.**—*See Antispasmodics.*

**Spermatorrhœa.**—*See Incontinence of Semen.*

**Sprains.**—Lin. Alb., Lin. Sap.; Lin. Succin. Co., Lin. Terebinth., Lin. Terebinth. Acet., Liq. Plumb. Subacet. Dil.; Lot. Evap., Lot. Plumb. c. Opio, Tinct. Arnica. Rad. (in a lotion), Tinct. Calend. (in a lotion), Ung. Sambuc.

**Sterility.**—Corpus Luteum, Ovarian hormones, Testicular Gland Sicc., Vitamin E preparations

**Stings.**—*See Bites.*

**Stomatitis.**—Potassii Chloras; Sodii Chloras; Sodii Thiosulphas (intravenously).

**Local.**—Acidum Boricum; Acidum Salicylicum; Acidum Sulphurosum; Alumen; Aluminii Aceto-Tartaras, Argent. Nit., Borax; Cupri Sulphas; Glycerinum and Mel Depuratum; Hydrargyri Perchloridum (1 in 5000); Iod. Colloid.; Liq. Calc. Hydrox., Collut. Liq. Hydrog. Perox.; Phenol, Potassii Chloras, Potassii Permanganas, Salol Mouth-wash; Sodii Chloras; Tinct. Myrrh. et Borac.; Trinitrophenol as paste (stomatitis mercurialis).

**Stomatitis, Gonococcal.**—Eyes, with 1 in 5000 Hydrargyri Oxycyanidum lotion. Urethra and mouth, 1 in 8000. Potassii Permanganas

**Styes.** **Local.**—Argenti Nitras; Copper Point or Cupri Sulphas Solution; Liq. Iodi Mit.; Ung. Hyd. Ox. Flav.; Zinci Sulphas.

Cerevisiæ Fermentum tablets combined with Lot. Acid. Boric. fomentations at night, frequent daily bathings with Lot. Acid. Boric., and incision of styte if matter forms, should effect cure.

**Styptics.**—*See Hæmostatics.*

**Sudorifics.**—*See* Diaphoretics.

**Sunburn and Freckles.** *Local*.—Acidum Lacticum (lotion), Æsculin 2% in Paraffinum Mollē or Pasta Hamamelidis; Liq Hydrarg. Perchlor.; Lot. Acid. Boric.; Lotio Calaminæ; Mist. Amygdal., Oleum Olivæ; Quinine in Past Hamam., Ung. Thor. Oleas diluted to a cream, Ung. Plumb. Carb.; Ung Salol cum Menthol.

Quinine the most effective protecting substance. The following pleasant to use Quininæ Dihydrochloridum 5, Aqua sufficient quantity to dissolve, Adeps Lanæ 40, Oleum Lavandulæ 1, Paraffinum Mollē to 100.

Acidum Tannicum 10, Alcohol 25, Aqua to 100. Apply freely to exposed parts of the skin before going out of doors.

**Sunstroke.**—Adrenalina, Apomorphina; Atropina, Bromides, Digitalis Folium, Hyoscina; Inj. Morph., Quinina, Strychnina; Veratrum; Venesection.

Sunstroke in the tropics cured by pilocarpine hypodermically with 1 or 2 minims of Oleum Crotonis.—J. McOscar, *Brit. med. J.*, ii/1923, 310.

**Sweating Feet.**—Aluminii Acetas; Liquor Formaldehydi, Pulv. Acid. Salicyl Co.

**Sycosis.** *Local*.—Acriflavina; Ichthammol, Iodides externally, Liq. Hydrarg. Perchlor.; Liquor Hydrogenii Peroxidi (diluted to 1 to 2 vols.); Liq. Plumbi Subacet., Mangani Butyras, Oleum Terebinthinæ (in oil injection); Staphylococcus Toxoid; Sulphur Sublimatum, Ung. Cupri. Oleas; Ung Hydrarg. Ammon.; Ung. Hydrarg. Nit. Fort., Ung. Hydrarg. Sulph. Flav.; Ung Thorni Oleas; X-Rays.

**Synovitis.**—Emp Hydrarg; Parogen Hydrarg, Ung. Hydrarg.; ¶ Ung. Hydrarg Co, Ung. Hydrarg. Oleat, Ung. Mercurial.

**Syphilis.**—Arsenical compounds; Arsphenamina Argentica; Bismuthi et Sodii Tartas; Bismuthi Salicylas; Bismuthi Subchloridum; Bismuthum Præcipitatum, Hydrargyri Iodidum Flavum, Hydrargyri Perchloridum, Hydrargyri Salicylas, Hydrargyri Subchloridum, Hydrargyrum, Neoarsphenamina; Potassii Iodidum; Sulpharsphenamina; Tryparsamidum.

*Local*.—Chromi Trioxidum, Garg. Chlor., Hydrargyri Cyanidum (in a paint, especially to throat and tongue), Hydrargyri et Zinci Cyanidum (in a gargle for sore throat, in an ointment for syphilitic sores), Hydrargyri Iodidum Flavum (in an ointment), Hydrargyri Iodidum Rubrum, Hydrargyri Nitras, Hydrargyri Oxidum Flavum, Hydrargyri Oxidum Rubrum, Hydrargyri Perchloridum, Hydrargyri Salicylas (as a dusting powder or in an ointment), Hydrargyri Subchloridum (as a dusting powder); Hydrargyrum Oleatum; Iodoformum; Iodum, Lot. Hydrarg. Nig; Resorcinol

**Tabes Dorsalis.**—*See* Locomotor Ataxia.

**Tachycardia.**—Amylis Nitris; Atropina, Cereus; Digitalis, Digitalinum (by injection), Liquor Glycyllis Trinitratis, Quinidinæ Sulphas, Sparteina, Strophanthinum, Strychnina.

**Tape-worm.**—*See* Anthelmintics.

**Tetanus.**—Antitoxinum Tetanicum, Amylis Nitris; Chloralis Hydras, Chlorbutol; Chloroformum; Conunæ Hydrobromidum, Curara, General Anæsthetics. Magnesi Sulphas (intraspinally); Nembutal; Morphina; Physostigminæ Sulphas (hypodermically).

**Tetany.**—A.T. 10; Calciferol; Calcium Salts, Parathyroideum

**Throat, Inflamed, and Tonsillitis.** *Internal.*—Acidum Acetylsalicylicum; Acidum Salicylicum and Salicylates; Aconitum; *p*-Aminobenzenesulphonamide; Belladonna; Catechu; Ferri Perchloridum; Guaiaci Resina; Kino, Kino Eucalypti, Krameria, Oxymel; Phenol; Potassii Chloras; Prontosil.

*Local.*—Acidum Tannicum; Benzoinum, Cocaina (in a spray), Ferri Acetas; Ferri Perchloridum (in a paint); Garg. Chlori, Garg. Pot. Chlorat.; Kino Eucalypti; Krameria (in a gargle); Liq. Calc. Chlorinat.; Menthol, Pasta Lindinensis; Phenol; Pig. Iodi Compositum; Potassii Nitras; Tab. Formaldehyd.

**Thrombosis, Coronary.**—Give Morphina freely,  $\frac{1}{2}$  to  $\frac{1}{4}$  grain subcutaneously or intravenously, then Tinct. Digit. in 20-minim doses every 6 hours up to 2 drachms (with care). Later give Theobromina et Sodii Salicylas 15 grains thrice daily.

**Thrush.**—*See* Stomatitis.**Tic Douloureux.**—*See* Neuralgia.

**Tinnitus Aurium.**—Acidum Hydrobromicum Dilutum; Pilocarpine injection.

Inflation of warm air, vapour of ether or chloroform, or a few drops of 5% methyl salicylate in liquid paraffin through a catheter.—*Lancet*, i/1926, 150.

**Digitalis Folium** in the pulsating form; Bromide (useful at bedtime and often gives great relief); hypnotics and sedatives, Oleum Iodisatum; Paraldehydum; Potassii Iodidum (where associated with vertigo), Pilocarpina (in cases showing Menière's symptoms); Thiosinamina (hypodermically).

**Tonics.** Heart.—Adrenalina, Æther, Alcohol, Ammonii Carbonas, Bari Chloridum; Caffeina, Caffeina et Sodii Benzoas, Caffeina et Sodii Salicylas, Camphora, Digitalis Folium, Digitalinum, Digitoxinum; Extractum Pituitarii Liquidum; Liq. Ammon. Dil., Nux Vomica, Quinidina, Quinidinæ Sulphas, Scilla; Strophanthinum; Strophanthus, Strychnina (and salts).

**Nerve**—Acidum Formicum (and formates), Acidum Glycerophosphoricum (and glycerophosphates), Acidum Hypophosphorosum (and hypophosphites), Arseni Trioxidum, Cinchona, Ferri Sulphas; Ignatia, Kola, Nux Vomica, Ovocleithrum; Phosphorus; Quinina (and salts); Strychnina (and salts).

**Stomach**—Acid Hydrochlor Dil.; Acid. Nitric Dil.; Acidum Nitrohydrochloricum Dilutum, Acid. Phosph. Dil., Acid Sulph. Aromat., Acid Sulph. Dil., Andrographis; Beberinæ Sulphas, Berberinæ Sulphas; Berberis, Calumba, Canella, Cascarilla, Chiretta, Cinchona, Cinchonidina, Cinchonina; Gentiana; Ignatia; Nux Vomica; Pepsinum; Picrorhiza; Quassia, Quebracha, Quinina; Rheum, Salix; Serpentaria; Taraxacum. (See also Carminatives.)

**Tonsillitis.**—See Throat, Inflamed, and Tonsillitis.

**Tonsillomycosis.**—Local application of Glycer Borac, Phenol Lotion 1 in 20, or diluted Liq. 18d. Mit. 1 in 2 Internally.—Acidum Acetylsalicylicum, Amidopyrina, Potassii Iodidum or Salicylates.—Sir A. Castellani, *J. trop. Med.*, Aug. 15, 1931, 275.

**Toothache.**—Camphora, Chloralis Hydras; Chloroformum, Chlorof. Camph., Cocaina; Collod. Carb., Cresotum, Menthol, Oleum Cari, Oleum Caryophylli; Phenol; Pig. Iod. et Aconit.; Res. Carb.; Tinct. Pyreth.

**Trachoma.**—Argentii Salts, Carboni Dioxidum (solid); Cupri Sulphas Oleum Chaulmoogræ rubbed into conjunctiva by a glass rod; Oleum Olivæ massage. Painting with Cupri Sulphas as satisfactory as any.

**Trypanosomiasis.**—Antypol, Antimonii et Potassii Tartras (in animals), Germanin, Moranyl, Neocryl, Tryparsamidum.

**Typhoid Fever.**—Acidum Salicylicum; Acidum Sulphurosum, Amidopyrina; Antityphoid Sera; Betanaphthol; Betanaphthylis Salicylas, Bismuthi Salicylas, Guaiacolis Carbonas, Hexamina; Hydrargyri Subchloridum, Magnesi Peroxidum (to arrest diarrhoea), Magnesi Salicylas; Naphthalenum, Oleum Terebinthinæ, Phenacetinum, Phenazonum, Phenol, Quininæ Salicylas, Sodii Phenolsulphonas; Sodii Salicylas; Salol, Vaccinum Typho-paratyphosum (as a prophylactic).

**Typhus.**—Æthylhydrocupreina, Morphina, Sodii Salicylas intravenously. See also Vol. II.

**Ulcers.**—Acidum Boricum, Acidum Salicylicum; Acidum Trichloraceticum (1% solution), Allantoinum, Alumen, Aluminii Sulphas (5 to 10% solution), Argentii Nitras, Bismuthi Carbonas, Bismuthi Oxyiodogallas (as dusting powder); Bromum (in a lotion); Calcii Chloridum (by intramuscular injection), Calcii Iodidum, Carbo; Chromii Trioxidum, Colophonium; Cysteine, Gelatinum Zinci; Electrotherapy, Hydrargyri Nitras; Iodoformum; Liq. Calc. Chlorinat., Liquor Hydrogenii Peroxidi; Liq. Sod. Chlorinat., Oleum Morrhuæ, Parathyroideum; Phenol; Plumbi Acetas; Plumbi Carbonas; Potassii Chloras (in a lotion), Potassii Hydroxidum; Rubrum Scarlatinum; Stannum, Symphytum; Thyroideum; Trypsinum (in an application); Ultra-Violet Light; Ung. Benzoini et Zinci; Zinci Chloridum (in a paste), Zinci Oxidum.

**Ulcers, Gastric and Duodenal.**—Acid. Hydrocyan. Dil.; Argentii Nitras; Atropina; Bism. Carb.; Calcii Carbonas; Calcii Chloridum; Calcii Phosphas; Ferri Perchloridum; Gelatinum; Glucosum Liquidum, Histidine Hydrochloride; Inf. Symphyt.; Kaolinum; Liq. Sod. Chlorid. Physiolog. injection; Magnesi Phosphas; Magnesi Trisilicas; Mist. Bism.; Mucin, Oleum Morrhuæ; Oleum Olivæ; Phenol et Morphina; Pulv. Bism. Co., Serum Normale.

(1) Promote healing by nourishing food, (2) "fix" the gastric acid and so prevent it from interfering with healing by ensuring that the food contains a large proportion of protein; (3) prevent distention of the stomach by small feeds. Milk and egg diet supplemented by iron and bismuth. Pain disappears early, vomiting quickly subsides and relapses are rare.

**Undulant Fever.**—Acriflavina intravenously, *Brucella melitensis* vaccine (see Vol. II); Fouadin; Intestinal Disinfectants, e.g., Betanaphthylis Benzoas;

Hexamina, Hexaminæ Salicylas; Salol Cerevisiæ Fermentum for peripheral neuritis of.

**Uræmia.**—Aconitum, Atropina, Bromides; Caffeina; Digitalis Folium, Erythritylis Tetranitras Dilutus, Liqueur Dextrosi et Sodii Chloridi, Liqueur Glycerylis Trinitratis, Liq Sod. Chlorid Physiol., Lithii Hippuras; Papaverina, Pilocarpina, Saline Purgatives, Scilla; Strophanthus, Venesection.

Treatment is unsatisfactory, as the underlying lesion is usually incurable and progressive. Only in acute nephritis can we expect to do more than stave off the fatal issue for a short time. The main indication is the elimination of toxins in every possible way. Diarrhœa should not be checked as it is nature's effort to get rid of toxins. Strong aperients and mercurial preparations are best avoided.—W. Langdon Brown and Geoffrey Evans, in Price's *Practice of Medicine*, 4th Edn., 1934.

**Urethritis.** *Local*—Argentii Nitras Irrigation (0.02 to 0.1%), or combined with Liqueur Hydrogenii Peroxidii (diluted to 1 to 2 volumes), Glycer Resorcin., Mangani Butyras (injection), Mercurochromum, Oleum Terebinthinæ (by catheter), Santalol (*per os*). *See also* Gonorrhœa.

**Uric Acid Diathesis.**—*See* Gout, Rheumatism.

**Urinary Calculi.**—*See* Calculi.

**Urine, to Render Acid.**—Acidum Hydrochloricum Dil., Acidum Mandelicum; Ammonii Chloridum, Ammonii Nitras; Ammonii Benzoas, Sodii Phosphas Acidus.

**Urine, to Render Alkaline.**—Calcii Carbonas, Lithii Carbonas, Lithii Citras, Potassii Carbonas; Potassii Citras; Sodii Bicarbonas, Sodii Citras, Sodii et Potassii Tartras.

**Urine, Incontinence of.**—*See* Incontinence.

**Urine, Retention of.**—Hexamina intravenously Glucosum Liquidum intravenous feeding.

*Post-operative retention of urine*—Pilocarpine intravenously  $\frac{1}{2}$  grain, or *per rectum*  $\frac{1}{2}$  grain, often successful where hexamine fails.

**Urine, Tests for Albumin, Sugar, etc.**—*See* Vol. II

**Urinary Antiseptics.**—*See* Antiseptics, Urinary.

**Urticaria.**—Acid. Hydrobrom. Dil.; Ammonii Bromidum, Calcii Chloridum, Calcii Lactas; Ergotamine Tartrate; Liq Adrenalina Hydrochloridi, Magnesii Carbonas Levis; Magnesii Carbonas Ponderosus, Magnesii Oxidum Leve, Magnesii Oxidum Ponderosum; Potassii Bromidum; Protein Therapy, Sodii Bicarbonas, Sodii Bromidum.

*Local*—Acidum Boricum, Acidum Hydrocyanicum Dilutum (in a lotion applied to the skin); Cocaina, Liq Plumb. Subacet. Dil.; Menthol, Potassii Carbonas (in a lotion); Sodii Bicarbonas (in a lotion).

**Uterus, Catarrh of.**—*See* Catarrh, Uterine.

**Uterus, to Promote Contraction of.**—Cimicifuga, Ergometrina, Ergota preparations, Ergotoxina, Gossypii Cortex; Hydrastis; Extractum Pituitarii Liquidum.

**Uvula, Relaxed.** *Local*—Alumen (gargle), Catechu, Ferri Perchloridum, Glycer. Acid. Tann., Kino, Krameria, Potassii Chloras, Troch. Acid. Tann., Troch. Kino, Zinci Chloridum or Zinci Sulphas (gargle or pigment).

**Varicose Ulcers.**—Calcii Chloridum; Calcii Iodidum, Parathyroideum; Ultra-Violet Light.

*Local*—Allantoinum, Gelatinum Zinci, Ligamentum Elasticum Adhesivum; Oleum Morrhuæ. *See also* Ulcers.

**Varicose Veins.**—*See* Sclerosants.

**Varicella.** *To prevent pitting.*—Argentii Nitras; Collod. Sinap.; Collod. Stypt.; Lin. Calc. Hydrox.; Liq. Iod. Mit.; Ol. Carbol.; Ung. Acid. Boric.; Ung. Hydrarg.; Ung. Zinc. Oleat. Potassii Permanganas (q.v.) Bath, 5% or less.

**Vasoconstrictors.**—Adrenalina; Caffeina (and salts); Digitalis Folium, Ephedrina (and salts), Ergota, Extractum Pituitarii Liquidum; Hydrastina, Nux Vomica, Strychnina (and salts).

**Vasodilators.**—Acetylcholina, Aconitum; Amylis Nitris; Benzoates; Erythritylis Tetranitras Dilutus, Ext. Thyroid. Liq., Liqueur Glycerylis Trinitratis; Pilocarpina; Sodii Nitris; Sodii Thiocyanas; Sparteinæ Sulphas; Sp. Æther Nitros.; Tab. Mannityl. Hexanit.; Yohimbina.

**Veneral Diseases.**—*See* Syphilis, Gonorrhœa.

**Vermicides, Vermifuges.**—*See* Anthelmintics.

**Vertigo.**—Acidum Hydrobromicum Dilutum (with a little Quinina);

Adrenalina (*per os*), Caffeina; Guarana; Quinina; Valerianas; Sp Ammon Aromat.; Strychnina, Tab Glyc. Trinit., Zinci Valerianas

**Vesical Catarrh.**—*See* Cystitis.

**Vesicants.**—*See* Counter-irritants.

**Vincent's Angina.**—Acetarsol; Sodii Perboras; Sodii Ricinoleas Mixture of Arsenic and Ipecacuanha, as also the Pig. Ipecac et Arsen. (*q.v.*).

Arsphenamina topically or thorough irrigation with Iodum, Acidum Trichloroaceticum; Liquor Hydrogenii Peroxidi (gargle), Sodii Perboras (paint and wash) said to be specific

**Voice, Loss of.**—Cocaina, Dec. Cetrar, Emuls. Ol. Morrhu.; Liq. Formaldehyd. Sap; Garg Phenol, Krameria, Menthol, Potassii Chloras and Borax, Solv. Borac. Co, Solv Pot. Permang, Tab Formaldehyd. (to suck). Amylis Nitris and other vasodilators in hysterical aphonia.

**Vomiting.**—Acidum Hydrocyanicum Dilutum; Ammonii Bromidum, Argenti Nitras; Bismuthi Carbonas; Bismuthi Subnitrates, Cerii Oxalas, Chlorbutol, Coca, Cocaina, Dextrosium, Extractum Suprarenali Corticis, Iodum, Liq. Calc Hydrox, Magnesii Carbonas Levis, Magnesii Carbonas Ponderosus, Magnesii Oxidum Leve, Magnesii Oxidum Ponderosum, Phenol; Potassii Citras; Sodii Bicarbonas; Sodii Phosphas

**Vomiting, Post-operative.**—Adrenalina *per os*, Chlorbutol, Cocaina subcutaneously For vomiting after chloroform a few drops of Chloroformum on Sugar

**Vomiting, Cyclic or Recurrent.**—Glucosum Liquidum injection Rectal feeding. Sodii Bicarbonas 1 drachm in Liq Sod. Chlorid. Physioli intravenously.

**Warts, Corns and Small Nævi.**—Acidum Aceticum Glaciale, Acidum Nitricum; Acidum Salicylicum, Acidum Trichloroaceticum, Argenti Nitras, Bismuthi et Sodii Tartras, Carboni Dioxidum (solid), Chromii Trioxidum, Collod. Salicyl Co; Cupri Oleas, Cupri Sulphas, Electrotherapy, Emp Salicyl Co. Fort.; Liquor Formaldehydi, Liq Hydrarg Nit Acid, Liq Sod Æthylat, Paraformaldehydum (25% in Collod. Simp), Phenol, Plumbi Oleas, Potassii Hydroxidum; X-Rays

**Wax in the Ears.**—Oleum Amygdalæ, then syringe or Liquor Hydrogenii Peroxidi, or diluted with an equal volume of glycerin, syringing afterwards; glycerin and saturated solution of sodium bicarbonate

**Whites.**—*See* Leucorrhœa.

**Whitlow.**—Liquor Hydrogenii Peroxidi, Mangani Butyras

**Whooping Cough.**—Acidum Benzoicum, Acidum Hydrocyanicum Dilutum, Æther (injections), Æthylis Iodidum (inhaled), Æthyl Morphina; Hydrochloridum, Ammonii Benzoas; Ammonii Bromidum; Atropina, Belladonna, Benzenum, Benzylis Benzoas, Bromoformum; Codeina; Coniina, Ephedrina, Ipecacuanha; Oleum Succini; Phenazonum; Potassii Bromidum, Sodii Benzoas, Sodii Bromidum, Syr. Bromof. Co.; Vaccinum Pertussis, Xylenum

**External.**—Baln. Vap Creosot.; Cresol (vaporised), Lin Succin Co; Resorcinol (in a spray); Vap. Coniin.

**Worms.**—*See* Anthelmintics.

**Wounds.**—Acidum Boricum, Acidum Salicylicum, Allantoin, Aluminu Acetas, Bismuthi Oxyiodogallas, Bismuthi Subnitrates, Chloramina, Cresol, Glycerinum; Hydrargyri et Zinci Cyanidum, Hydrargyri Perchloridum; Iodoformum; Liq. Calc. Chlorinat. c. Acid. Boric., Liquor Formaldehydi, Liq Sod. Chlorinat Chir; Liq. Sod. Chlorinat. c. Sod. Bicarb.; Oleum Morrhuæ, Phenol; Rubrum Scarlatinum; Sal Alembroth, Sodii Sulphas; Symphytum, Viride Malachitum; Viride Nitens, Zinci Chloridum. *See also* Antiseptics.

**Yaws.**—Acetarsol, Arsphenamina, Arsphenamina Argentica, Bismuthi Arsanilas; Bismuthi Subgallas; Injectio Bismuthi, Neoarsphenamina; Sodium Potassium Bismuthyltartrate; Sulpharsphenamina, Ung. Bism. Subchlor

**Local.**—Ung. Hydrarg. Nit. Fort. (1 in 3 Paraffinum Mollé).

**Yellow Fever.**—Serum of convalescent patients tried. *See* Vol. II.

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